The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 115, NO. 25 — COPYRIGHT, 1940, BY AMERICAN MEDICAL ASSOCIATION CHICAGO, ILLINOIS — DECEMBER 21, 1940

SHOULD SERUM BE USED IN ADDITION TO SULFAPYRIDINE IN THE TREATMENT OF PNEUMOCOCCIC PNEUMONIA?

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The value of specific serum in the treatment of pneumococcic pneumonia has been recognized for many years. Recently the effectiveness of sulfapyridine in this disease has become equally well established. The indications for the employment of each of these therapeutic agents, the methods of administration, the results to be expected from their use and the possible toxic effects are by now almost universally known. What is not known, however, is the relative value of the two agents when either is used alone or when they are administered in combination.

In table 1 are shown the results of treatment with serum alone as compared with those following treatment with sulfapyridine alone in several clinics where comparative studies have been made. Pneumococci of all types were represented among the causative agents in these cases. Volini, Levitt and Campione [1] reported that 15, or 9.8 per cent, of 153 patients treated with specific serum died, as compared with two (3.3 per cent) deaths among 60 sulfapyridine-treated patients. Although complete data are not given, the disease seems to have been of equal severity in the two groups.

We [2] found a 16.7 per cent mortality rate, sixteen deaths among 96 patients treated with serum alone, as compared with a mortality rate of 11 per cent, fifteen deaths among 136 patients treated with sulfapyridine alone. The pneumonias were considered to be of approximately equal severity in the two groups, although there were possibly a few more mild pneumonias in the sulfapyridine-treated than in the serum-treated group.

Finland, Spring and Lowell [3] treated 211 patients with specific serum, of whom 28, or 13.3 per cent, died. Among 225 patients treated with sulfapyridine alone, 40 died, giving a mortality rate of 17.8 per cent. The authors state that at first sulfapyridine was given only in the milder cases but that later its use was extended to all cases.

Ruegsegger, Hamburger and Cockrell [4] reported a series of cases which had been treated alternately with serum and with sulfapyridine, respectively. Two (4.4 per cent) of 45 patients treated with serum died and 6 (12 per cent) among 49 patients receiving sulfapyridine. The age distribution of the patients and the percentage of patients with bacteremia was approximately the same for the two groups.

Bullowa and his co-workers [5] rotated patients after type identification, treating some with serum alone, others with sulfapyridine alone, and others with the combination of the two. There were nineteen deaths among 111 patients treated with serum alone—a mortality rate of 17.3 per cent. Among the 124 patients treated with sulfapyridine alone, 10, or 8.1 per cent, died.

Among a total of 616 patients treated by all these investigators with serum alone 80, or 13 per cent, died; while among the 594 patients treated with sulfapyridine alone 73, or 12.3 per cent, died. As measured by mortality rates, therefore, the results of patients treated with sulfapyridine alone are approximately the same as those following treatment with specific serum alone.

Since sulfapyridine has been found to influence recovery from pneumonia by causing bacteriostasis of the pneumococci [6] and since it apparently does not increase antibody formation in the host,[7] one may assume that specific serum, by introducing passive antibodies into the host, would be a valuable adjunct to

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Cooperation was given by Dr. G. C. Ruhland, Dr. J. G. Cumming and Dr. J. E. Noble, of the Health Department of the District of Columbia, and by the resident staff of Gallinger Municipal Hospital. Technical assistance was given by Miss Emily Godfrey and Mr. Norman E. Yongue.

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drug therapy. In order to test this hypothesis, Spring, Lowell and Finland [8] performed in vitro experiments by means of the pneumococcidal test. They found that killing of pneumococci occurred more readily when specific serum and sulfapyridine were used in combination than when either one was used alone. Bullowa and his associates [5] reached the same conclusion by the use of bone marrow cultures of pneumococci.

Several investigators have studied this problem in animals. Maclean, Rogers and Fleming [9] found that 25 mg. of sulfapyridine was insufficient to protect mice injected with 100 minimum lethal doses of type VIII pneumococci. When mice were vaccinated with killed pneumococci of the same type and seven days later given 100 minimum lethal doses they likewise died. However, if mice were vaccinated and seven days later received the infecting dose and also sulfapyridine, all of them survived. They were apparently fortified with antibodies from the vaccination and in addition had the advantage of the bacteriostasis caused by the drug.

TABLE 1.—*Pneumonia Patients Treated with Serum Alone Compared with Those Treated with Sulfapyridine Alone*

Reported by	Specific Serum			Sulfapyridine		
	No. of Cases	No. Died	Per Cent Died	No. of Cases	No. Died	Per Cent Died
Volini et al.[1]	153	15	9.8	60	2	3.3
Dowling and Abernethy [2]	96	16	16.7	136	15	11.0
Finland et al.[3]	211	28	13.3	225	40	17.8
Ruegsegger et al.[4]	45	2	4.4	49	6	12.0
Bullowa et al.[5]	111	19	17.3	124	10	8.1
Total	616	80	13.0	594	73	12.3

Kepl and Gunn [10] produced pneumonia in rats with type I pneumococci and treated some with sulfapyridine alone, some with serum alone and others with a combination of the two. Measured by mortality rates and by the length of survival among the animals that died, the best results were obtained in the group which received both serum and sulfapyridine. However, when Wright and Gunn [11] used the same methods to produce pneumonia with type III pneumococci there was no significant difference in the mortality rate following the use of serum and sulfapyridine combined, as compared with the mortality rate following the use of sulfapyridine alone.

Powell and Jamieson [12] infected groups of rats intraperitoneally with type I, II, V, VII, VIII and XIV pneumococci. In all types, with the possible exception of type VIII, the combination of sulfapyridine and specific serum resulted in a higher percentage of survivals than either agent used alone.

MacLeod [13] found that sulfapyridine and serum were synergistic in infections caused by type III pneumococci in mice, since the number of survivors was greater when the combination was used for treatment than when either agent was used alone.

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In view of the favorable results obtained by using serum in addition to sulfapyridine in vitro and in animal infections, the present study was undertaken to determine whether the same synergistic action would be obtained in a series of patients with pneumonia caused by pneumococci of types I through VIII.

MATERIALS AND METHODS

The patients were alternated between sulfapyridine therapy and specific serum plus sulfapyridine, as follows: As soon as a patient was admitted to the wards of Gallinger Municipal Hospital and the diagnosis of pneumonia suspected, the sputum was typed and a blood culture taken. No treatment, other than symptomatic, was given until a pneumococcus or other etiologic organism was obtained. If a pneumococcus belonging to one of the first eight types was identified, alternate treatment was given within each type, one patient being given sulfapyridine alone and the next sulfapyridine plus specific antipneumococcus serum.[14] No exceptions to the strict alternation of cases were made on the basis of severity of the disease. Occasionally, when a patient was demonstrated by means of intradermal and intravenous tests to be hypersensitive to both horse and rabbit serum, that patient was given sulfapyridine alone and the next two patients in sequence were given the combination of sulfapyridine and serum, so that the series might be even again. This procedure was also employed for the few occasions when a patient had been started on one or the other therapeutic regimen and was subsequently found not to have pneumonia. A patient receiving any serum which was subsequently discontinued because of hypersensitiveness was nevertheless classified as having received combined therapy. If no type of pneumococcus was obtained from the sputum within six hours, treatment with sulfapyridine was begun and the case entirely omitted from the series.

TABLE 2.—*Mortality Rates of Pneumonia Patients Treated with Sulfapyridine Alone and in Combination with Specific Serum*

Type	Sulfapyridine			Serum Plus Sulfapyridine		
	No. of Cases	No. Died	Per Cent Died	No. of Cases	No. Died	Per Cent Died
I	23	3	....	22	2	....
II	9	0	....	10	0	....
III	15	4	....	16	5	....
IV	6	1	....	6	0	....
V	3	0	....	3	0	....
VI	2	1	....	2	0	....
VII	13	1	....	13	1	....
VIII	9	0	....	10	0	....
All cases	80	10	12.5	82	8	9.8
All except type III	65	6	9.2	66	3	4.5

There was no fixed dosage schedule for serum. The initial dosage was usually 100,000 units, but often a larger or smaller initial dose was given, depending on the severity of the illness and the duration at the time treatment was begun. If the patient did not show considerable improvement within twelve to twenty-four hours, or if pneumococci were cultured from the blood stream, additional serum was given. The average total dosage of serum per patient was 141,000 units. Thus it is evident that these patients received about the same doses of serum that they would have been given if serum had been administered without sulfapyridine.

14. Supplied by the Lederle Laboratories, Inc., through the courtesy of Dr. W. G. Malcolm.

The initial dose of sulfapyridine was 4 Gm. by mouth, followed by 1 Gm. every four hours until the temperature reached normal and remained so for three or four days. From that point on, the dose was gradually decreased and the drug finally discontinued after about six days of normal temperature. In the more severely ill patients the first treatment consisted of an intravenous injection of from 3.5 to 4 Gm. of sodium sulfapyridine.

TABLE 3.—*Effect of Certain Factors on Mortality Rate*

	Sulfapyridine			Serum Plus Sulfapyridine		
	No. of Cases	No. Died	Per Cent Died	No. of Cases	No. Died	Per Cent Died
Age of the patient						
12 to 39	49	0	0	54	3	5.5
40 and over	31	10	32.3	28	5	17.8
Percentage over 40	38.6	..	....	34.1	..	....
Area of lung involvement						
One lobe	60	8	13.3	64	2	3.1
More than 1 lobe	20	2	10.0	18	6	33.3
Percentage over 1 lobe	25.0	..	....	21.9	..	....
Blood culture						
No bacteremia	62	7	11.3	66	6	9.1
Bacteremia	18	3	16.7	16	2	12.5
Percentage bacteremic	22.5	..	....	19.5	..	....
Day treatment begun						
First 4 days	47	3	6.4	38	1	2.6
Fifth day or later	33	7	21.2	44	7	15.9
Percentage after 4th day	41.3	..	....	53.6	..	....
Complicating diseases						
Uncomplicated	66	4	6.1	65	1	1.5
Complicated	14	6	42.8	17	7	43.7
Percentage complicated	17.5	..	....	20.7	..	....

Whenever the oral administration of sulfapyridine resulted in low blood levels, it was supplemented by the sodium salt intravenously unless the temperature had already fallen and remained down. The average total dose of sulfapyridine per patient was 40 Gm. among the patients receiving the drug alone and 36.9 Gm. among the patients receiving serum in addition.

RESULTS

In table 2 are shown the mortality rates by type. There were ten deaths among the 80 patients treated with sulfapyridine alone—a mortality rate of 12.5 per cent. Among the 82 patients treated with the combination of serum and sulfapyridine there were eight deaths, or 9.8 per cent. In each group of cases caused by an individual type of pneumococcus (with the exception of the cases caused by type III pneumococci) the mortality rate was the same or lower for patients treated with the combined method than for those treated with sulfapyridine alone. If the type III cases are excluded, there were six, or 9.2 per cent, deaths among the 65 patients treated with sulfapyridine and only three, or 4.5 per cent, among the 66 patients treated with sulfapyridine plus serum.

Thus it appears that when a comparison is made of the sulfapyridine-treated group as a whole with the combined therapy group as a whole, only a slight difference in mortality rate is evident in favor of the combined therapy group. However, when an analysis is made of the cases on the basis of several factors of importance in pneumonia, differences between the two groups become more apparent. These factors, which are shown in table 3, are age of the patient, area of lungs involved, the presence of bacteremia, the day of the disease on which treatment was begun and the presence of complicating diseases.

These data show, first of all, that the cases in the two groups were of about the same degree of severity. While a slightly higher percentage of patients treated with the drug alone (as compared with those given the combination therapy) were over 40 years of age, had more than one lobe involved and had organisms in the blood stream, on the other hand a slightly higher proportion of patients receiving the combination treatment were treated after the fourth day of the disease and had other diseases complicating the pneumonia. These complicating conditions included acute alcoholism, congestive heart failure, diabetes mellitus, uremia, asthma, tuberculosis and pregnancy.

Among the patients under 40 years of age there were no deaths in the group of 49 who received sulfapyridine alone and only three (or 5.5 per cent) in the group of 54 patients who received serum plus sulfapyridine. There was a more striking difference among the patients over 40 years of age. Of the 31 patients in this group who received sulfapyridine alone 10, or 32.3 per cent, died, while among the 26 patients receiving serum plus sulfapyridine there were five, or 17.8 per cent, deaths. Thus the mortality rate of patients over 40 years of age was nearly twice as great for patients receiving sulfapyridine alone as for patients receiving sulfapyridine in combination with serum.

There were eight deaths (13.3 per cent) among the 60 patients in the sulfapyridine-treated series with one lobe involved and two, or 3.1 per cent, deaths among the 64 patients with one lobe involved who were given combined therapy. When more than one lobe was involved, the mortality rate was greater for those treated by the combined method (33⅓ per cent) compared with 10 per cent for those given the drug alone.

There was little difference in the two groups in relation to the presence or absence of bacteremia. There was an 11.3 per cent mortality rate among the sulfapyridine-treated patients with negative blood cultures and a 9.1 per cent mortality rate among those treated with serum plus sulfapyridine. In the group with bacteremia, 16.7 per cent of those receiving the drug alone died and 12.5 per cent of those receiving the drug plus serum.

Only 1 patient died (2.6 per cent of 38 cases) whose treatment with the combination of drug and serum was begun in the first four days of the disease, while 3 patients, or 6.4 per cent, died among the 47 given the drug alone at this stage of the disease. Among the cases in which treatment was begun after the fourth day of the disease, 21.2 per cent died when treated with sulfapyridine alone and 15.9 per cent died among those treated with sulfapyridine plus serum.

TABLE 4.—*Rapidity of Crisis*

Method of Treatment	No. of Patients Recovering	Crisis in 12 Hours		Crisis in 24 Hours	
		Number	Per Cent	Number	Per Cent
Sulfapyridine	70	12	17.1	28	40.0
Serum plus sulfapyridine	74	28	37.8	44	59.5

Among the patients whose pneumonia was uncomplicated by any other disease, 4 (or 6.1 per cent) died after receiving the drug alone, and only 1 (or 1.5 per cent) died among those receiving the drug plus serum. The mortality rates for the patients who suffered from other diseases along with pneumonia were practically the same for the two groups: 42.8 per cent for those receiving the drug and 43.7 per cent for those receiving combination therapy.

In table 4 is shown the relative speed with which the temperature reached a permanent level below 100 F. in the two groups. Within twelve hours after treatment was begun the temperature was below 100 in 12, or 17.1 per cent, of the 70 patients who recovered after treatment with sulfapyridine alone, as compared with 28, or 37.8 per cent, of the 74 patients who recovered after the combined treatment. After twenty-four hours the percentage of patients whose temperature was below 100 F. was still greater (59.5 per cent) in the group receiving sulfapyridine plus serum than it was (40.0 per cent) in the group that received sulfapyridine alone. These rapid crises occurred more frequently in the patients who received the combined treatment in spite of the fact that many of the sulfapyridine-treated patients received their initial dose of sulfapyridine by vein, whereas the initial intravenous dose was seldom given to the patients who received serum also.

COMMENT

On the basis of the results obtained in vitro and in animal experiments, one would expect to find, among patients treated with serum plus sulfapyridine a definite lowering of the mortality rate below that obtained when sulfapyridine was used alone. The two studies reported in which cases of pneumonia have been rotated for treatment by these two regimens do not seem to bear this out. Don and his associates [15] reported on patients with type I and II pneumococcus pneumonia alternated in this manner. Among 49 patients who received sulfapyridine alone only 1 died, whereas there were three deaths among 37 patients treated with sulfapyridine plus specific serum. However, the dose of serum used was small, since patients under 40 years of age admitted within ninety-six hours of the onset received only 50,000 units and all other patients 100,000 units. No additional doses were given regardless of the course of the disease. This dosage would not be considered adequate for many patients receiving serum alone as treatment for pneumonia. Furthermore, the authors state that patients admitted during the night were started on sulfapyridine immediately and typing was postponed until the following morning. One wonders whether the treatment in the combined serum-sulfapyridine cases would not have been more effective if treatment with the two agents had been commenced at the same time.

Bullowa and his associates [5] gave sulfapyridine to 124 patients, of whom 10, or 8.1 per cent, died, while 89 patients were treated with serum plus sulfapyridine with ten, or 11.2 per cent, deaths. When patients treated in the first four days of the disease were considered, there were five deaths among 53 patients given sulfapyridine alone and only one death among the 39 patients treated with sulfapyridine plus specific serum.

Our results show a slightly lower mortality rate when serum was used in addition to the drug than when sulfapyridine was used alone. When the type III cases are omitted, the results are still more favorable for the combined therapy group. The omission of type III cases may well be justified on the ground that there is no report, as far as we are aware, of any significant group of type III cases in which the mortality rate has been definitely lowered by serum therapy. On the other hand, the prognosis in this type of pneumonia is particularly poor, the mortality rate being as high as, or higher than, that for pneumonia caused by any other type of pneumococcus. Even when sulfapyridine is administered, the death rate is still high. In our own experience there have been fourteen deaths, or 22.6 per cent, among a total of 62 type III pneumonias treated with sulfapyridine, alone or in combination with serum. These facts should stimulate further attempts to lower the mortality rate in this type of pneumonia by combined serum and sulfapyridine therapy.

Although bacteremia is one of the factors which profoundly affect the prognosis in pneumonia, the results obtained in the present series seem to show that sulfapyridine is equally effective when used alone or combined with serum. It has been repeatedly recommended that serum be given in addition to sulfapyridine when bacteremia is present. Our observations tend to question the necessity for this, unless other factors which make for a poor prognosis are present.

Serum seems to be particularly effective as an adjunct to sulfapyridine in patients over 40 years of age and in patients with only one lobe involved, especially when these patients are treated early in the disease. Since the death rate from pneumonia has been repeatedly found to increase progressively with the age of the patient, the superior advantage of combined therapy in the older age group is most welcome.

The relative cheapness and ease of administration of sulfapyridine will make it the method of choice in all cases except those in which it is definitely contraindicated. If our results are confirmed by other similar studies, they would suggest that every patient over 40 years of age seen within the first four days of the disease receive serum in addition to sulfapyridine. After the fourth day of the disease the value of serum as an adjunct is less. In order to give the patient the benefit of every possible aid, however, massive doses of serum might be given along with sulfapyridine to severely ill patients seen late in the disease. Sputum should be obtained for typing and blood taken for culture in every case before sulfapyridine is started, so that serum may be given, whenever it is indicated, as soon as the type is determined. This is necessary in order that the utmost advantage may be taken of the superior results achieved by the earliest possible administration of serum.

SUMMARY AND CONCLUSIONS

1. A series of cases of pneumonia caused by pneumococcus type I through type VIII have been alternated for treatment with sulfapyridine alone and with sulfapyridine plus specific antipneumococcus serum. The mortality rate was 12.5 per cent in the group receiving sulfapyridine alone and 9.8 per cent in the group receiving serum plus sulfapyridine. If the type III cases are omitted, the corresponding figures are 9.2 and 4.5 per cent, respectively.

2. Serum seemed to be particularly valuable as an adjunct to sulfapyridine in patients over 40 years of age.

3. Crisis occurred more frequently and was more prompt in the patients receiving serum in addition to sulfapyridine.

4. It is suggested that serum and sulfapyridine both be given to patients over 40 years of age with pneumonia and to those who are in need of a prompt defervescence.

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EARLY OPERATION (SPINE FUSION) IN UNSTABLE LUMBOSACRAL JOINTS

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The problem of treating patients with the primary complaint of low back pain, often with sciatic radiation, continues to harass the orthopedic surgeon. This is true not only because of the difficulties in diagnosis so aptly expressed by Steindler [1] when he states that "It [backache] shares with the symptoms of headache the distinction of having almost unlimited possibilities of interpretation" but also because "So long as surgeons disagree in regard to the pathogenesis of chronic low back pain, there cannot be any uniformity of opinion concerning treatment" (Compere [2]). In spite of these limitations, the orthopedist is repeatedly called on to determine the etiology of this syndrome and then must he decide on whether to follow conservative or radical therapy.

Among younger patients with low back pain due to an unstable lumbosacral joint we at the clinic have been impressed with the results obtained from lumbosacral fusion and dismayed by the difficulty of achieving relief of symptoms through conservative methods on older poor risk patients who likewise exhibit an unstable lumbosacral articulation as well as marked degenerative changes in this area of the spine. It therefore occurred to me that some worth while information might be gained through a study of two groups of patients with low back pain due in my opinion to similar etiology—an unstable lumbosacral joint: group 1, older persons who had received conservative treatment over a period of years of which one year, if not the entire interval, was under personal supervision; group 2, younger patients treated by arthrodesing operations. Obviously, the two groups of patients are not directly comparable, but there is a definite similarity in respect to the history of onset and subsequent backache symptoms during the same age cycle, together with the degree of disability in this period which offers a reasonable basis for study. To clarify the situation, no patient is included with a clinical history or physical examination (including lumbar puncture, and, when indicated, spinogram study) that indicated herniation of an intervertebral disk.

GENERAL CONSIDERATIONS

Space does not permit a detailed discussion of the anatomic, physiologic and pathologic (as far as is known) factors of low back pain. These aspects have been extensively discussed in the literature. However, certain general considerations may be stated that indicate the basis for the approach to the problem.

I agree with Willis [3] that "to understand properly the anatomical structures of the lower back and to appreciate its susceptibility to aches of obscure etiology, consideration must begin with the manner in which the lower extremities become attached to the vertebral column. In the evolution of man the pelvis has progressed toward the head by incorporation of the sacrum and successive last number of vertebrae, the next preceding segment thereupon assuming the characteristics of the last lumbar segment." Of particular interest are the variations in the formation and articulation of the last lumbar and first sacral segments, where anomalies are common to all vertebrates and are, in the main, steps in an evolutionary shortening or lengthening of the presacral column. Variation in the number of presacral segments is of little importance in a discussion of backache, whereas the presence of asymmetrical sacralization and defective lumbosacral articulations is of definite interest in that they provide points of lessened resistance to stress and strain and, with a definite susceptibility, to muscle and ligament injury. Furthermore, the lumbosacral region is inherently weak "because as a structure developed for quadrupedal function with a support under either end of it [the spine] has been forced to manage a right angle turn and balance in the upright position, thereby acquiring mechanical imperfection and areas of exaggerated stress."

I therefore support the clinical concept advanced by Ferguson [4] in 1925 and published in 1934 that lumbosacral anomalies produce symptoms only through faulty mechanics. As long as the muscles and ligaments are of sufficient strength and tone to enable the person to continue in his environment without fatigue there are no symptoms; that is, the patient is "compensated." Decompensation, and hence back pain, results from failure of the muscles and ligaments to support the lumbosacral area. This is particularly prone to occur in a spine which exhibits faulty mechanical structure because these muscles and ligaments "have less than normal capacity for meeting extraneous stress and strain since a certain portion of their total capacity is already in use." This conception is especially well borne out in the type of case here reported (group 1), which illustrates the fact that as one grows older the muscles lose their tone and power. In consequence, the person well compensated at 20 may at 40 not have sufficient muscle power to protect the lower part of the back from strains that were easily met in earlier years.

Since the principal cause of low back pain in these cases is fatigue strain in the soft tissues resulting from

Fig. 1.—The arrows indicate the most stable type of lumbosacral articular facets, namely when the articular surfaces face internal-external in relation to the midline of the body.

From the Department of Bone and Joint Surgery, the Lahey Clinic.
Read before the Section on Orthopedic Surgery at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

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4. Ferguson, A. B.: The Clinical and Roentgenographic Interpretation of Lumbosacral Anomalies, Radiology **22**: 548 (May) 1934.

the structurally faulty mechanical construction or abnormally close relations of the bony parts, such a condition will often affect one side more than the other, or even one side alone. Furthermore, symptoms from the stress and strain need not be on the same side as the bony anomaly, for the most potent irritating factor is not

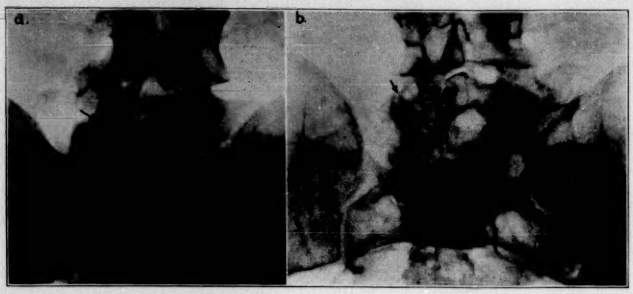

Fig. 2.—*a*, Unstable asymmetrical lumbosacral articular facets with rudimentary articular processes. *b*, Another example of very unstable asymmetrical facets, the joint surfaces facing superior-inferior. Note productive bone change about these articulations.

necessarily the most obvious anomaly in the roentgenogram. Badgley [5] and Hodges and Peck [6] also emphasized this point in a study of 447 patients, of whom 27 per cent who complained of low back pain had anomalies of the lumbosacral region as opposed to 14.3 per cent with anomalies in a symptom-free control group.

DEFINITION

The term unstable lumbosacral joint is descriptive of a clinical entity which includes any arrangement of bony parts at the lumbosacral junction that is not adequate for support without undue stress or strain on the adjacent muscles and ligaments (Ferguson). Such an arrangement comprises one or more of the following mechanical faults: unstable lumbosacral facets (including rudimentary articular processes), bone defects in the posterior elements of the lumbosacral vertebrae, transitional vertebrae (sacralization and lumbarization), spondylolisthesis, abnormally acute lumbosacral angle and posterior displacement of the fifth lumbar vertebra on the sacrum.

A narrow lumbosacral disk may also be observed. Two types are recognized. One is congenital and is found in normal sacralization wherein the vertical diameter of the disk may vary between the diameter of the usual thick lumbosacral type and that of the thin sacral disk, as pointed out by Willis. It is doubtful whether this type is a cause of pain. The second type is acquired and is due either to trauma, such as a heavy fall on the buttocks, or to degenerative changes in the disk, the result of faulty posture. Williams [7] believes that this condition explains posterior displacement of the fifth lumbar on the first sacral vertebra, because settling of the disk segment takes place in a down and backward plane guided by the inclination of the sacral facets, and the more acute the lumbosacral angle the more marked is the posterior tilt of the first sacral facet and thus the greater the posterior displacement of the fifth lumbar vertebra.

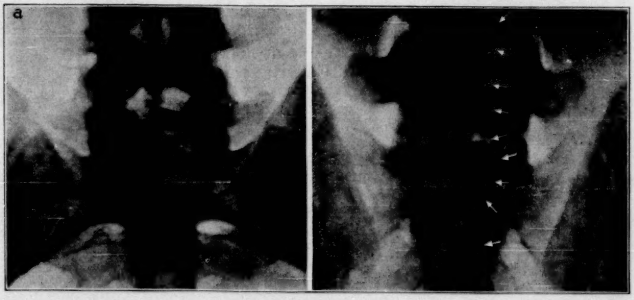

Fig. 3.—Bone defect in posterior elements of the lumbosacral vertebra. *a*, Usual anteroposterior view. *b*, View at 45 degree angle, same patient, illustrating the effective value of this film to show the defect.

POSTERIOR DISPLACEMENT OF THE FIFTH LUMBAR VERTEBRA

It is my opinion that posterior displacement of the fifth lumbar vertebra on the sacrum is an entity and not an illusion. Repeated study of roentgenograms indicates that the decision on this point lies in obtaining true lateral views of the lumbosacral area. When one is in doubt as to the presence of this anomaly, as these displacements are variable, a comparison of true lateral roentgenograms in extreme flexion and again in hyperextension of the lumbosacral spine and hip joint will decide the question.

Ferguson states that the mechanism of posterior displacement of the fifth lumbar vertebra on the sacrum occurs as follows: In the presence of a hypermobile lumbosacral joint due to the coronal type of articular facets, on hyperextension the fifth lumbar glides backward on the first sacral vertebra—an exaggeration of the normal motion—while on flexion, instead of gliding forward, the fifth lumbar tilts forward as it is caught in the position of posterior displacement. Finally I believe that, as a minimum, 95 per cent of patients with chronic low back pain are best treated by a conservative regimen. This statement does not include pathologic conditions of the spine such as tuberculosis, primary neoplasms, fractures, osteitis or her-

5. Badgley, C. E.: Clinical and Roentgenographic Study of Low Back Pain with Sciatic Radiation: A. Clinical Aspects, Am. J. Roentgenol. **37**: 454 (April) 1937.

6. Hodges, F. J., and Peck, W. S.: Clinical and Roentgenographic Study of Low Back Pain with Sciatic Radiation: Roentgenological Aspects, ibid. **37**: 461 (April) 1937.

7. Williams, P. C.: Lesions of the Lumbosacral Spine: Acute Traumatic Destruction of the Lumbosacral Intervertebral Disks, J. Bone & Joint Surg. **19**: 343 (April) 1937; Chronic Traumatic (Postural) Destruction of the Lumbosacral Intervertebral Disks, ibid. **19**: 690 (July) 1937.

niated disks. Thus among 2,000 patients with pain low in the back who were seen at the clinic from January 1936 to January 1939 fifty, or 2.5 per cent, were submitted to arthrodesing operations.

But it is also my opinion that in emotionally balanced younger patients of the age group from 30 to 45 years with persistent low back pain due to an unstable lumbosacral joint, and in whom a trial of adequate conservative therapy has not been successful, fusion of this articulation should be offered as a preferred method of treatment. Arthrodesis is indicated rather than to have the patient accept an often marked degree of permanent limitation of activities while he continues to experiment with various supports and different forms of physical therapy, as well as visiting a series of physicians in his effort to be rid of periodic bouts of severe low back pain.

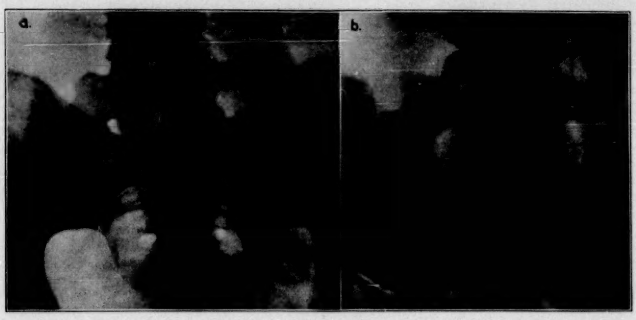

Fig. 4.—*a*, Transitional vertebra illustrating unilateral incomplete sacralization. Note rudimentary type of articular processes and also the bone condensation about pseudarthrosis. *b*, Three years after lumbosacral spine fusion. Complete relief of low back symptoms of four years' duration in a woman aged 32. Note also that the sacralized process has fused to the sacrum.

ANALYSIS OF CASES

GROUP 1.—Herewith is a summary of the observations on seventy-five patients (fifty-four women, twenty-one men), average age 52, who had experienced disabling low back pain owing to an unstable lumbosacral joint over a period of from ten to fifteen years. In every case there was roentgenographic evidence of productive bone changes at the unstable articulation. Generalized degenerative arthritis of the lumbar spine was noted in eighteen cases of this group. This consistent finding of degenerative bone changes about unstable lumbosacral joints is significant not only as indicative of the mechanical unsoundness of the joint but also because this arthritis, when established, is an additional factor in the production of symptoms. Such arthritic pain would in turn have been avoided by a fusion operation earlier in life.

The onset of persistent low back symptoms in this group occurred in the age interval of 30 to 40 years; 85 per cent were between 31 and 35 years old. The fourth decade is the period when previously well functioning (that is, compensated) muscles and ligaments begin to weaken from lack of use. Then decompensation of these soft parts takes place and back symptoms result. It is also important to bear in mind not only that these patients have experienced years of low back pain with attendant repeated efforts to ameliorate symptoms but also that in this interval all have accepted a definite reduction in the degree of their usual physical activities. This limitation is well expressed in the summary of the words of one patient: "I realized I had a weak back and therefore avoided activities that I thought might cause an acute attack or intensify my chronic low back pain."

The treatment of these patients in this clinic as well as elsewhere included all the methods of conservative therapy with which we are familiar. Of effective methods there was one common denominator, namely bed rest. In many instances it is quite probable that persons would have experienced comparatively slight disability if they had carried out instructions consistently, especially in regard to muscle exercise and diet to reduce weight. But in our experience it is an exceptional patient who for years will follow such a regimen. Therefore, a younger person with low back pain due to an unstable lumbosacral joint not relieved by a trial of conservative therapy, should, I believe, be asked seriously to consider and, if possible, have a fusion operation performed, because a lumbosacral arthrodesis, when successfully carried out, eliminates the etiologic mechanical factor as well as preventing development of degenerative arthritic changes at the lumbosacral joint.

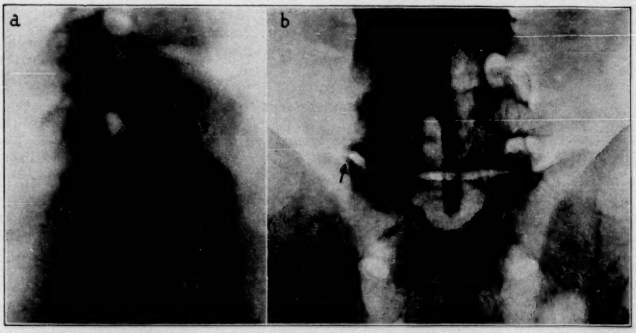

Fig. 5.—*a*, Illustrating definite posterior displacement of the fifth lumbar vertebra on the sacrum, with narrow intervertebral disk. Marked disability in a man aged 45. *b*, Anteroposterior view of the same patient. Note productive bone changes about the unstable lumbosacral articular facets which are of the anteroposterior type.

GROUP 2.—The following data summarize the results of arthrodesing operations on fifty patients (thirty-four

women, sixteen men), with an average age of 36 years, all with severe low back pain due to an unstable lumbosacral articulation. The average age at onset of symptoms was 32 years. Each of these patients had received an adequate trial of conservative therapy without permanent relief. Forty-six patients, or 92 per cent, were relieved of their back symptoms after spine fusion (from eighteen months to three years follow-up). There were four failures due to poor selection of cases. Two patients exhibited chronic arthritis originally thought to be localized at the lumbosacral joint but which proved to be a progressive process and spread to other levels of the spine. One patient was definitely a psychiatric subject, and this condition was not recognized in time to prevent the operation, and one patient who has a compensation problem has obtained no relief and, in my opinion, will not until definite arrangements are made for a pension. A postoperative roentgenogram on this patient shows a firm fusion.

CONCLUSIONS

1. The majority of patients with chronic low back pain can be relieved of their symptoms by conservative measures.

2. As a result of experience with one type of case—in which symptoms are due to an unstable lumbosacral joint—I believe that if a definitive trial of conservative treatment does not relieve symptoms, or if the mechanical arrangement of the bony part is very faulty, as for example in pronounced spondylolisthesis, then an arthrodesis of the lumbosacral spine is the best method of treatment.

Spine fusion is indicated because in these cases the pain and disability result from failure of the adjacent muscles and ligaments to support the back, owing to fatigue in consequence of the underlying faulty mechanical construction or abnormally close relation of the bony parts. Such decompensation of muscles and ligaments usually occurs between the ages of 30 and 45 and is most frequently observed from 34 to 39 years, when the person is no longer physically as active and hence muscle tone and ligament support are not so effective as in the younger age group.

3. While my experience with compensation cases has not been extensive, I agree with Compere that these patients are best considered for spine fusion after financial settlement has been made, unless there are marked abnormal changes at the lumbosacral junction.

4. Arthrodesis of the spine for low back pain is contraindicated in the emotionally unstable or psychiatric patient, as well as in the elderly person.

605 Commonwealth Avenue.

ABSTRACT OF DISCUSSION

DR. ALLEN F. VOSHELL, Baltimore: I am in accord with the principles given by Dr. Haggart under his conditions and only wish all would as carefully limit themselves as he has done. I wish he had reviewed his ideas on the "compensation back" and applied his fundamentals thereto. Not only is the diagnostic decision exceedingly difficult in this group but more so is treatment whether conservative or operative. The use of the same treatment for a noncompensatory as for a compensatory patient will most times result in an entirely different outcome. Almost all his cases are of the nonindustrial type, which might have some bearing on the speed of recovery and the high percentage of excellent results. I should like to ask whether his four cases of failure to recover and improve were due to nonfusion or to some other reasons. What type of fusion was followed? And over what area? Was the postoperative care associated closely with muscle building and was physical therapy carefully controlled? If so, for how long?

DR. FREDERICK A. JOSTES, St. Louis: Most orthopedic surgeons who have had the opportunity to fuse lumbosacral joints because of backache have encountered the great difficulty presented by the compensation boards, insurance companies and the like. Some insurance companies have come to the point where they have flat-footedly said that no fusion shall be done in any patient of theirs. That, in my estimation, is a wrong attitude. However, before a radical procedure such as a spinal fusion is offered to a patient, one should offer him adequate conservative treatment, including firm support in the way of a bed and a brace, and his activity at least during that period should be limited. The burden of proof is on the man who sees the patient in his first attack of backache. I am certain that chronicity of back conditions may depend very much on the initial treatment. Such patients should have the usual supportive measures, gentle manipulation and complete rest for at least several days. It is most difficult to get these patients to rest, especially if one has been able promptly to relieve them of acute pain by manipulative procedure. Much time from usual activity and loss of working hours could be avoided in this way and recurrences are less apt to happen. It seems only fair that in selected cases in which extraneous factors such as compensation diseases or escape mechanisms have been definitely ruled out, given a young individual or even an older one who has repeated attacks of pain, repeated loss of time from whatever activity the patient indulges in or one who must so completely limit his activities as to interfere with his normal way of living, even though one can relieve him promptly of his pain in each attack, such persons should be offered the opportunity to be made free from attacks and pain and limitation of activity by a fusion operation. As suggested, compensation cases might be done after a settlement has been made. Promiscuous fusion, of course, is to be condemned.

DR. G. E. HAGGART, Boston: I did not go into the technical aspects of the fusion operation because of limited time. The fusion in these cases was performed on the lumbosacral joint except in patients with spondylolisthesis, where the fourth lumbar vertebra was included. The Hibbs technic, slightly modified, was employed. We do not transplant bone from the tibia as has been done in the past, but we do secure additional bone from the posterior superior iliac spine which can be exposed through the same incision, swung slightly to the side from which the bone is to be taken. The iliac spine is exposed by dissecting free the skin and subcutaneous tissue from over this area; the bone directly underneath is then denuded of soft parts, and it truly offers a "well" from which it is possible to obtain a large amount of soft medullary bone shavings which, when packed about the lumbosacral facets, are extremely helpful in producing rapid fusion. The length of time patients were kept in bed postoperatively was a minimum of six weeks; the average is seven. When the patient had to leave the hospital (via ambulance) for financial reasons or any other factors, he remained in bed at home a minimum of eight weeks. Just before he is allowed up the patient is fitted with a Taylor type back brace. While in bed he has not worn a support but lies on a firm fracture bed. This is much more comfortable than wearing a cast or brace in bed, which I do not think is necessary. When the patient is ambulatory, the Taylor back brace is worn three months on the average. In some instances it has been much shorter. This decision obviously depends on what the postoperative roentgenogram reveals, and we are guided by that together with the general condition of the patient. The point Dr. Voshell brings up about exercises is significant. Obviously, a back will not function simply because one has an internal bone splint. It is also essential to have muscle power. None of these patients were operated on until they had completed a preliminary interval of muscle training, which likewise they carried out after operation. The point I wish to emphasize about this group of individuals in their thirties with low back pain due to an unstable lumbosacral joint is that if they have developed in that age period severe disabling back pain and if a definitive, that is, a limited period of conservative therapy is not successful in relieving symptoms, then I believe the question of a fusion operation should be considered. In my opinion these patients should be advised to have an arthrodesis of the lumbosacral joint.

THE PATHOLOGY AND TREATMENT OF OBSTRUCTIONS AT THE VESICAL NECK IN WOMEN

HUGH H. YOUNG, M.D.
BALTIMORE

The pathology and treatment of obstructions at the vesical neck in women and the inflammatory conditions that lead up to them have received scant attention in the American literature. Two years ago I was able to collect and present thirty-six cases. I showed that the development of hesitation, difficulty in starting micturition, slowness of the stream, irritation, pain, hematuria and the presence of more or less complete retention of urine are quite similar to those conditions in men. On cystoscopic examination the mucosa of the urethra and adjacent portion of the trigon is inflamed, often edematous or even papillomatous. The trigon sometimes hypertrophies as a result of the obstruction. The bladder becomes trabeculated and sometimes cellular from back pressure and increased activity of the detrusors. Impairment of renal function may result from residual urine and back pressure effects on the ureteral orifices and the consequent dilatation of the ureters, pelves and thinning of the renal cortex. With

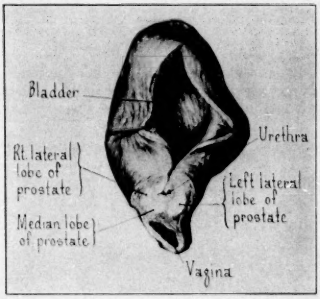

Fig. 1.—Autopsy specimen showing cross section of a prostate of almost normal male dimensions from a female with virilism due to adrenal hyperplasia.

the advent of infection the condition becomes aggravated and ultimately the results may be very serious.

I found that Caulk [1] was apparently the first to report the removal of the obstruction in one of these cases. He employed his cautery modification of my punch instrument. Since then other urologists have employed my simple cold cutting punch, the fulgurating punch of Thompson or the electrical resector of McCarthy. A few operators have attacked the obstruction suprapubically by excision or enucleation. Folsom and others have held that glands which they found in the region of the vesical neck of the female urethra are largely responsible for the persistence of inflammatory conditions and for the development of obstruction. In 1853 Virchow first noted stones in the female urethral glands resembling those found in the male prostate. He concluded that they were homologous structures. Since then many others have held that certain structures in the female urethra are homologues of the male prostate. Tourneux (1889), Magee (1892), Pallin (1901) and Eratt (1911) reported finding the presence of prostatic homologues in varying amounts along the entire female urethra. Eggerth (1915) pointed out that the anlage of the bulbo-urethral gland (Cowper's gland) and the major vestibular glands (Bartholin's glands) of the human embryo are homologous.

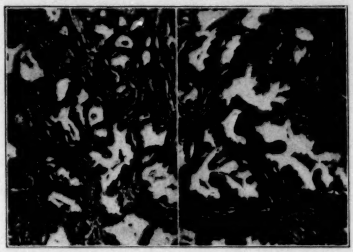

Fig. 2.—Appearance of two sections of a large prostate from a female with adrenal hyperplasia.

In 1922 Johnson,[2] working in this clinic, made the most exhaustive embryologic study of the vesical neck in the female. He made serial sections of female embryos of various lengths (60, 75, 150, 215 and 275 mm.) and from these prepared wax reconstructions that showed glands along the urethra from the vesical orifice to the meatus which, he asserted, corresponded to the prostatic glands in the male. Johnson asserted positively that "the whole homologue of the prostate in the female was here demonstrated for the first time." Johnson also studied by serial sections the glands of the

Fig. 3.—Section showing glands beneath urethra in vesical neck which correspond to prostatic glands in the male.

adult female urethra and concluded his study with the statement that the urethra in the female corresponded with that portion of the male urethra which lies between the prostatic orifice and the utricle.

Coincidentally with the formation of prostatic glands in the male, similar glands appear in the female. These prostatic glands in the female correspond in number

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

Read before the Section on Urology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Caulk, J. R., and Patton, J. F.: The Cautery Punch Operation for the Removal of Obstructive Lesions at the Vesical Orifice in Women and Children, J. Urol. **33**: 504-512 (May) 1935.

2. Johnson, F. P.: The Homologue of the Prostate in the Female, J. Urol. **8**: 13-34 (July) 1922.

and give rise to branches, but they never attain the development of the male prostatic glands except when, as a result of hyperplasia of the adrenal cortex (the androgenic zone), these prostates in females continue their growth and ultimately almost attain the development of the male prostate. In the normal female these glands, according to Johnson, differ from the prostatic glands in being fewer in number, being less closely packed together, having fewer branches and showing much less evidence of active secretion. In "Genital Abnormalities: Hermaphroditism and Related Adrenal Diseases" I [3] presented autopsies on three female pseudohermaphrodites in which great enlargement of the adrenals was found. In between the cortex and the medulla there was a tremendous development of the androgenic zone of Grollman characterized by the presence of many fuchsinophil cells. In these cases the prostate was considerably developed. The prostate from one of these patients is shown in figure 1. As seen here this patient, a woman of 26, had a prostate of almost normal male proportions. In figure 2 are shown sections of the prostate from another one of these patients. The similarity to the normal male prostate is evident.

At my request Dr. John Haines has secured sections from routine autopsies in the department of pathology. In figures 3 and 4 the typical appearance of these periurethral glands in the female is seen. The important role played by inflammation involving the urethra and the periurethral glands in the female is shown in the following case:

A woman aged 66 was admitted with complete retention of urine of eight months' duration. For a time there had been marked nausea, vomiting and severe uremia. She then began a catheter life and when she came to us her bladder was being emptied four times a day. Cystoscopy showed a contracted vesical neck with a posterior bar that was identical in appearance with that frequently seen in the male. The trigon was hypertrophied and the bladder was trabeculated and held 500 cc. of residual urine. With my cold cutting punch the obstruction was removed in three cuts. The patient left the hospital able to void normally and has now been followed for nine years.

Fig. 4.—Section showing suburethral glands near vesical neck, homologues of prostatic glands in the male.

The operative result is considered perfect. Photomicrographs of the tissue removed by the punch instrument in this case are reproduced in figures 5 and 6. As seen here, considerable inflammation of the periurethral glands in the formation of marked fibrosis is present.

3. Young, H. H.: Genital Abnormalities: Hermaphroditism and Related Adrenal Diseases, Baltimore, Williams & Wilkins Company, 1937.

This case is somewhat similar to others that we have studied. In most instances the obstruction has not been so complete or the gradual development so pronounced. In some much more fibrosis is present. In all it seemed evident that chronic inflammation played an important part in the case. We have in our files the

Fig. 5.—Section of tissue removed by punch operation on a woman with obstruction to urination (complete retention). Glands homologous to prostate surrounded by chronic inflammation and bar formation are seen.

case histories of some 500 women suffering with inflammatory conditions varying in degree at the vesical neck and the adjacent portion of the urethra. The

Symptoms of Chronic Urethritis (Nonspecific) in Women (101 Cases)

	Cases
Frequency	78
Burning	31
Urgency	26
Backache	24
Hematuria	16
Pain in renal region	15
Suprapubic pain	20
Painful urination	15
Bearing down feeling	13
Pain in bladder	9
Difficulty or hesitancy in voiding	9
Incontinence	7
Straining on urination	2
Cloudy urine	1
Bladder tenesmus	1
Leukorrhea	1
Painful coitus	1

symptoms noted in the 101 cases studied in detail are given in the accompanying table.

On cystoscopic examination with the right angle telescope one sees only the conditions within the bladder at the vesical orifice. In the presence of a contracture or a bar, either posterior (fig. 7) or anterior, the condition is easily seen with this type of telescope. For lesions farther out in the urethra my antegrade telescope or the fore-oblique telescope of McCarthy is essential. With these instruments one sees all degrees of inflammatory change from simple urethritis to edema, irregular swellings of the mucous membrane, definite cysts and polypoid growths of varying degree (fig. 8). Rarely ulceration is present. The entire urethra generally shows a marked reddening and evidence of chronic inflammation. With the instrument in the urethra and a finger in the vagina, thickening of the urethra, par-

ticularly at the vesical neck, is often demonstrable. In some cases a definite stricture is present. Caruncles are not infrequently seen at the urethral meatus.

These cases present a common and often very troublesome condition in women that is often overlooked. The fact that the urine is usually normal, the cultures grow no bacteria and the ordinary cystoscope shows a vesical orifice that appears normal with the right angle telescope has led many observers to pronounce the urethra normal and to seek to relieve these patients by ureteral instrumentation. This is particularly true when pain in the back with attacks of colic in the region of one or both kidneys strongly suggests ureteral and renal abnormality. Benefit following cystoscopy and ureteral dilation not infrequently has been accepted as confirming the diagnosis, but such benefit may indeed be the result of urethral instrumentation rather than ureteral. As shown in 101 cases analyzed, the symptoms are apparently localized quite a distance from the urethra. It is therefore highly essential that, even when the history of the patient seems to point strongly to disease of the upper urinary tract, a very careful study of the urethra should be made, and if evidence of chronic inflammation and the various pathologic conditions described are present local treatment for the urethra and vesical neck is indicated, certainly as a preliminary measure before the patient is subjected to a series of ureteral dilations or operations on the kidney itself.

CONCLUSIONS

Chronic inflammatory conditions in the female urethra, especially in the deep portions and at the vesical neck, are common in women. They are accompanied by symptoms that are often referred to regions higher up in the urinary tract. In most cases, however, local symptoms are present in the urethra and bladder. Chronic inflammatory changes in the mucous membrane, in periurethral structures and particularly in the glands are often present and evinced by swelling, by edema, by cystic and polypoid formations and sometimes

Fig. 6.—Section showing fibrosis at vesical neck and submucous glands homologous to prostate.

by the development of definite bars or contractures of the vesical orifice. For the proper study of these cases an antegrade or fore-oblique telescope or urethroscope is essential. These lesions may often be missed during the course of cystoscopy with the right angle telescope. The conditions which produce such severe local and referred symptoms are readily cured by endourethral treatment: applications of silver nitrate, fulguration, the punch operation or excision of the obstructing bar, or severely inflamed regions either with the simple punch instrument or the electrical resectoscope. Care must be taken not to overdo lest

Fig. 7.

Fig. 8.

Fig. 7.—Cystoscopic view of rounded bar at vesical neck of a woman which caused marked obstruction to urination.

Fig. 8.—Urethral polyps just below vesical neck due to chronic inflammation. These are easily destroyed by fulguration or simply by applications of silver nitrate stick.

incontinence for a time may occur. Accurate and adequate endoscopic methods often clear up these long standing and troublesome conditions.

ABSTRACT OF DISCUSSION

DR. HENRY DAWSON FURNISS, New York: I have been familiar with the work on the glands of the urethra; a German some years ago reported that he had found in some of these glands corpora amylacea. However, I don't believe I have seen exactly the kind of cases that Dr. Young reports. I have seen many cases of urethral obstruction with the retention and pathologic condition of the upper urinary tract; also patients with residual urine which I thought was more apt to be due to some cord lesion than to any obstructive lesion in the urethra itself. I see a few cases of urethral stricture, but even with those with rather marked obstruction I do not see much evidence of retention or urinary tract infection. Dr. Emmet, of the Mayo Clinic, recently brought out that in many of these cases retention of urine is due to a disproportion of the expulsive force of the bladder and the retentive force of the sphincter; that when the retentive force is disproportionately greater than the expulsive force there is retention and residual urine. I shall be on the lookout for the type Dr. Young has described. My experience has been mostly that in cases of retention there are cord lesions.

DR. ALF F. GUNDERSON, La Crosse, Wis.: Dr. Young has called attention to an important condition which the average urologist rarely has occasion to see. The total number of reported cases of true intrinsic bladder neck obstruction in the female numbers only about 50 cases. The diagnosis is not difficult but one must exclude (1) gynecologic conditions such as uterine tumors and cystocele, (2) intra-urethral pathologic conditions—strictures, urethral diverticula, polyps, (3) intravesicular tumors and (4) hysteria. After exclusion of these factors one is aided by cystoscopy. Observers write about a bar, a ridge, fibrous contracture, hypertrophy of the internal sphincter that one can easily see through a cystoscope. I am impressed with the paucity of actual visible abnormality in the bladder neck in such cases. I would sound a note of warning! The female sphincter as seen through a urethroscope is often deceiving and gives one the impression of being the seat of a bar or contraction. One should attach greater importance to evidence of obstruction as found in the bladder—residual urine, trabeculation, saccules—rather than the appearance of the bladder neck. The amount of tissue present as an obstructing factor is truly disappointing. There is no uniformity of opinion with regard to the causation. Infection with resultant fibrosis and contracture with occasional hyperplastic glandular structures has been the generally accepted course of pathologic events. This theory was advocated by Caulk, Folsom, Van Houton and

others. However, Braasch and Thompson have been unable to demonstrate a greater amount of fibrosis in the removed tissue than there is present in the normal female bladder neck at necropsy. A greater amount of inflammatory cells has been seen as well as some hypertrophy of the epithelium and muscle bands. These observers feel that the inflammation, although the exciting cause, does not adequately explain the true basic etiology. They suggest an associated neurogenic cause: a nervous unbalance between the sphincteric musculature and the detrusor muscle which leads to a spasm of the sphincter, and subsequently to hypertrophy, and, finally, occasionally to active hyperplasia of the muscle. More evidence has accumulated to support this hypothesis by recent information obtained in the treatment of the neurogenic bladder or tabetic bladder by resection of the internal sphincter. Emmet in a recent publication has brought this forcibly to our attention. Resection of the sphincter as advocated by Caulk, Thompson, Emmet and others is merely an effort to facilitate emptying of the bladder by weakening one muscle against another or creating a more favorable muscle balance or readjustment.

DR. EDWARD N. COOK, Rochester, Minn.: The paucity of evidence that we see on cysto-urethroscopic examination around the bladder neck is the most interesting part to me of this problem. We must depend on our history concerning obstructive difficulty, small stream, frequent passage of the urine and occasionally the association of burning, the presence of residual urine and the appearance on cystoscopic examination, not at the bladder neck but rather in the bladder itself, such as trabeculation and cellule formation. This condition is worthy of our very careful consideration. It is true that not many cases have been reported. Thompson reported 24 at the Quebec meeting. We have had 12 cases since that time. Of interest is the fact that in most cases only a small amount of tissue will need to be removed. Occasionally one or two bites or nothing more than a sphincterotomy at times will relieve these patients of their symptoms. They are a group which have been treated unsatisfactorily for a long while, and I think we should pay more attention to them. As regards the pathologic conditions found I have not been particularly impressed with the amount of fibrosis and have not felt that this could be attributed to an inflammatory process; first, because of the fact that the inflammatory process in the female urethra is notoriously a frequent occurrence and yet obstruction in the female urethra is notoriously rare. Second, if one will examine the tissue removed in these cases and also examine postmortem tissue from the urethra in females that never had any difficulty with urination one will see little or no difference. It is possible that hypertrophy of the sphincter muscle as a result of spasm is the most common cause of the condition. In some cases a neurogenic dysfunction has led to sphincteric hypertrophy in my opinion.

DR. T. LEON HOWARD, Denver: If Dr. Folsom were here he would greatly appreciate the fact that Dr. Young has substantiated his observations, for he has insisted for many years that these are true glands and that they are often infected. Dr. Young's sections have proved that this is a fact. It seems to me that I see these patients every day. Others see them too, but if one is attempting to view the urethra and bladder sphincter with an ordinary Brown-Buerger cystoscope one is passing over the pathologic condition. If there is a disease condition present and one uses a fore-oblique lens cystoscope, there will be no difficulty in locating it and opening or destroying the polypoid-like growths with a fulgurating wire. This condition often begins during childhood, and patients go through life suffering from its effects. Pyelitis in children is frequently the result of infected glands in the posterior urethra, and until one cures these glands one cannot cure the pyelitis. Many pediatricians have failed to recognize this. It is astounding how many females have residual urine caused by these obstructing polypoid growths. If you suspect that they have residual urine and want to prove it easily, put ordinary liquid petrolatum in the bladder. If there is residual urine you will find liquid petrolatum floating on top of the next catheterized specimen whether it is obtained at the end of a week or a year. There is no guesswork about this test in either the male or the female patient.

DR. HUGH H. YOUNG, Baltimore: I have purposely not discussed cases in which there were spinal cord and other neurologic lesions present. These cases belong to a separate group. With proper urologic methods, including cystometric studies, they can be differentiated from the inflammatory and obstructive conditions to which I have limited my paper. Dr. Howard has emphasized the fact that with the ordinary cystoscope many of these conditions at the vesical neck in women are missed. My antegrade telescope or McCarthy's fore-oblique will show very well these changes at the vesical neck and in the deep urethra in women. They are indeed quite common and are responsible for many referred pains as well as many errors in diagnosis. I saw a woman recently who came because she had seizures of severe pain in the vesical neck. The ureters had been dilated many times; she had received orthopedic treatment, bladder lavage and stretching without relief. I found pronounced inflammatory conditions at the vesical neck with a little obstructive bar and much glandular inflammation. A small punch operation and treatment of the posterior urethritis with silver nitrate cured her completely. Another woman with very severe bladder and back pains had a large polyp and other inflammatory conditions deep in the posterior urethra and vesical neck. She had become a morphine habitué as a result of years of suffering. Local treatment relieved her. My simple tubular endoscope with application of silver nitrate, either by means of the stick or by means of 20 per cent solution on swabs, is usually entirely effective. Too much deep resection or fulguration is not advisable. When there is definite obstruction, the resection which I have described is very effective.

DIASTASIS OF THE DISTAL TIBIOFIBULAR JOINT AND ASSOCIATED LESIONS

RUFUS H. ALLDREDGE, M.D.
NEW ORLEANS

Diastasis of the distal tibiofibular joint is associated with extensive ligamentous rupture and results from external rotation or abduction injuries at the ankle. It may occur without associated fracture but is more frequently seen in cases of Pott's fracture in which there is fracture of the internal malleolus or rupture of the internal lateral ligament together with fracture of the lower third of the fibula. There may also be a fracture of the posterior aspect of the tibia extending into the joint.

Most articles in the literature on fractures of the ankle with rare exceptions [1] direct attention to the fractures of the malleoli and posterior tibial margin, leaving the impression that diastasis is of secondary importance. Undoubtedly failure to recognize and treat properly the diastasis may result in permanent disability even when the associated fractures are accurately reduced.

An effort has been made in this presentation to call attention to some practical points of importance regarding rupture of the distal tibiofibular ligaments and the associated injuries.

ANATOMY AND PHYSIOLOGY OF THE TIBIOFIBULAR JOINT

It is necessary here to review briefly the anatomic structures of the ankle joint which have direct bearing on the subject under consideration.

From the Department of Surgery, Division of Orthopedic Surgery, Tulane University of Louisiana School of Medicine and Charity Hospital and Touro Infirmary.

Read before the joint meeting of the Section on Surgery, General and Abdominal, and the Section on Orthopedic Surgery at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. Merle d'Aubigné, R., and Smets, W.: Les formes frustes de déplacement externe de l'astragale dans les fractures malléolaires, Presse méd. **42**: 157, 1934. Apfelbach and Boim.[2]

There is a definite but atypical articulation between the distal tibia and fibula, and the synovial membrane usually extends up between these two bones for a distance of about one-fourth inch.

Fig. 1.—End result of unrecognized and untreated tibiofibular diastasis compared to the normal ankle. Note osteo-arthritis and narrowing of joint space. Ankle fusion was necessitated by complete disability.

The distal ends of the tibia and fibula are bound together by rather weak ligaments. These ligaments are (1) the anterior lateral malleolar (anterior inferior tibiofibular ligament), (2) the posterior lateral malleolar ligament (posterior inferior tibiofibular ligament), (3) the transverse ligament, which is an extension of the posterior lateral malleolar ligament, and (4) the interosseous ligament, which is a direct extension of the interrosseous membrane extending downward to the

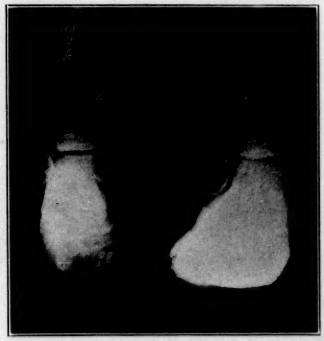

Fig. 2.—Normal amount of separation of fibula from tibia when foot is dorsiflexed. Left, plantar flexion. Right, dorsiflexion. Note difference in width of tibiofibular joint space.

synovial cavity. The latter is longer in front than behind and occupies the space between the anterior and posterior malleolar ligaments.

Because the astragalus is 25 per cent wider in front than behind, it is necessary for fibular motion of some type to take place at the ankle mortise when the foot is dorsiflexed, even though the mortise is also slightly wider in front than behind. Just what these motions are has not been clearly described. It has been said [2] that the fibula glides upward on its long axis when the foot is dorsiflexed and downward when it is plantarflexed. Efforts in this study to confirm this view have been unsuccessful. Measurements of x-ray films taken on the normal proximal and distal ends of the fibula do not show any movement in its long axis on extreme motions of the foot. It must be concluded, therefore, that the fibula does not glide upward or downward in its long axis.

It has been shown by taking anteroposterior x-ray films on the normal ankle that definite widening of at least 2 to 3 mm. takes place at the tibiofibular joint when the foot is dorsiflexed. Slight anteroposterior motion of the fibula has also been demonstrated at the lower tibiofibular joint by inspection of the fresh specimen. When the tibiofibular ligaments are sectioned, the fibula separates abnormally from the tibia when on dorsiflexion the foot reaches 90 degrees. The clinical importance of this fact will be indicated later.

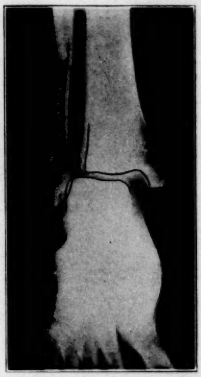

Fig. 3.—Gross tibiofibular diastasis. Note abnormal width of joint space between internal malleolus and astragalus, loss of parallelism of joint lines of lower tibia and astragalus, and lateral displacement of astragalus.

DIAGNOSIS OF TIBIOFIBULAR DIASTASIS

Clinical signs and symptoms of rupture of the ligaments and diastasis of the tibiofibular joint depend on the extent of injury and whether associated fracture is present. Frequently, when associated with a Pott's fracture, the signs and symptoms of the fracture completely overshadow those of tibiofibular ligament rupture and diastasis. Swelling and tenderness over the distal tibiofibular joint may be indicative when the fracture of the fibula is fairly high. This sign is of no value when the external malleolus is fractured. Gross ballottement of the fibula may rarely be present. Widening of the malleoli and abnormal anterior and posterior motions of the fibula may be seen when the ligaments are extensively torn.

Proper x-ray examination is important in every case. The preliminary use of local anesthesia may facilitate the taking of proper views. The x-ray examination should be considered as an adjunct in diagnosis and the surgeon should, if possible, be present when the x-ray films are made so that proper views will be assured. All anteroposterior views of the ankle joint should be taken with the malleoli equidistant from the x-ray film. The following views should be taken in all doubtful cases: (1) anteroposterior with the foot plantarflexed; (2) anteroposterior with the foot dorsiflexed; (3) anteroposterior view with the foot in external rotation; (4) lateral view with the foot in neutral position. If the usual anteroposterior and lateral views show dis-

2. Apfelbach, George, and Boim, Leon: Fractures of the Ankle. Arch. Surg. **35**: 328-357 (Aug.) 1937.

tinctly the exact nature of the lesion and especially if gross diastasis is present in these views, the others may be omitted. Fluoroscopic examination is probably not as accurate as the examination of carefully taken x-ray films in the various positions.

A thorough understanding of the mechanism of fractures about the ankle is a prerequisite to proper interpretation of the x-ray films. It should be kept in mind that extensive ligamentous injury is as important as bony injury and may be diagnosed from the x-ray films alone.

The presence of an isolated fragment of bone between the distal tibia and fibula is a positive sign of diastasis and results from ligamentous avulsion of the outer border of the tibia. Rupture of the tibiofibular ligaments with diastasis is present in most cases in which there is a fracture 2 or 3 inches above the lower tip of the fibula associated with fracture of the internal malleolus or rupture of the internal lateral ligament.

Widening of the space between the internal malleolus and the internal aspect of the astragalus when the

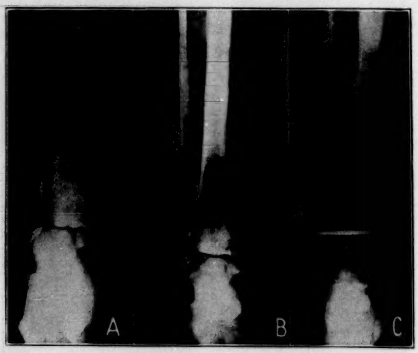

Fig. 4.—*A*, note in addition to all signs indicating tibiofibular diastasis the fragment of bone avulsed from the lateral aspect of the tibia. *B*, same case after attempted closed reduction. Loose fragment of bone became interposed between the fibula and the tibia. *C*, same case after operative removal of loose fragment and fixation of fibula to tibia by means of a vitallium screw. Note accuracy of reduction of internal malleolus. It reduced spontaneously when the fibula was approximated to the tibia.

internal malleolus is not fractured indicates both a rupture of the internal lateral ligament and tibiofibular diastasis when the fibula fracture is fairly high.

Normally the external border of the astragalus is in line with the external line of the tibia and any deviation of this normal alinement to the lateral side indicates lateral displacement of the astragalus. Diastasis is a frequent cause of lateral displacement of the astragalus.

In the normal ankle the joint lines between the lower tibia and the superior border of the astragalus are parallel. Diastasis with lateral displacement of the astragalus is a frequent cause of loss of parallelism of these lines. Fracture of the internal and external malleolus or rupture of the internal lateral ligament are other causes of loss of parallelism of the joint lines.

Gross diastasis of the mortise with marked widening between the tibia and the fibula are usually recognized without difficulty. Complete diastasis with interposition of the talus is rare and occurs only when the ligaments and interosseous membrane are completely torn. In doubtful cases x-ray films of the normal ankle in plantar flexion and dorsiflexion compared with those of the injured ankle may be of aid. The normal amount of widening when the foot is dorsiflexed should be kept in mind.

TREATMENT

Treatment of rupture of the tibiofibular ligaments and diastasis should be based on anatomic and physiologic considerations, taking into account the normal motions at the tibiofibular joint. The importance of early recognition and treatment cannot be overestimated. Apfelbach and Boim [2] in 300 films of ankle fractures noted diastasis in 40 per cent at the time of injury, whereas widening of the mortise was observed in 94 per cent as a clinical end result.

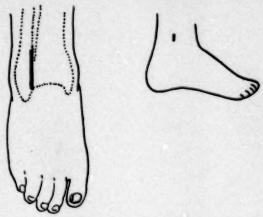

Fig. 5.—Incision for approach to tibiofibular joint and also small buttonhole incision through which metal fixation is inserted when necessary.

It must be kept in mind that not only widening of the ankle mortise but anteroposterior instability of the distal end of the fibula may result if diastasis is not recognized and properly treated. If normal motions and ankle joint stability are to be preserved, early accurate reduction must be carried out and maintained until the ligaments and the associated fractures have healed.

In the presence of definite tibiofibular diastasis the tibia and fibula may be reapproximated readily, provided there is no interposition of soft tissue or bone. When difficulty is encountered in effecting reduction, interposition is usually found to be the cause. Organized clot may give the same effect in late cases. Operation should be resorted to without hesitation under these

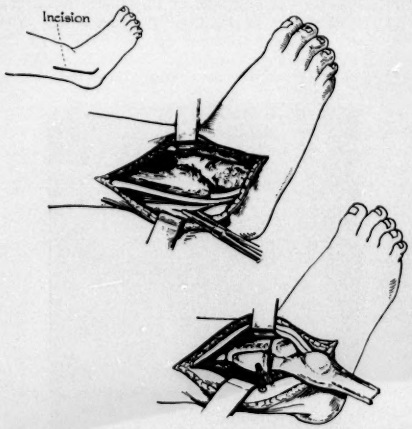

Fig. 6.—Gatellier's approach to posterior tibial marginal fracture. Indicated when closed reduction is unsuccessful and when there is complete rupture of the tibiofibular ligaments. In addition, the internal malleolus may be approached through a separate medial incision if necessary.

circumstances and the interposed substance removed or accurately replaced. The approach is made through a short incision over the anterior aspect of the tibiofibular joint. If difficulty is encountered in holding the fibula in its place well against the tibia, a screw or wire may be inserted through a small incision on the lateral aspect of the fibula.

The question of the routine use of metal fixation of the fibula to the tibia is one that has not been definitely settled. Undoubtedly it may facilitate the handling of these cases in some instances. One may cause fractures of the internal malleolus with gross displacement to reassume readily the normal relation to the tibia simply by reducing the diastasis and adequately maintaining reduction by the use of a screw. Removal of the metal fixation should be carried out in every case as soon as the ruptured ligaments have healed. Failure to do so usually results in the loss of dorsiflexion because motions of the fibula are prevented when it is fixed to the tibia.

The position in which the foot is immobilized after reduction has been effected is of importance whether internal fixation is used or not. It has already been brought out in this study that separation of the mortise after the ligaments are divided takes place when on

Fig. 7.—*A*, tibiofibular diastasis, fracture in the lower fourth of the fibula, fracture of internal malleolus and posterior tibial marginal fracture. Closed reduction unsuccessful. *B*, after operation. Gatellier's approach used. Tibiofibular screws should always be removed when union has occurred.

dorsiflexion the foot reaches 90 degrees. The position of choice for postreduction immobilization then is slight plantar flexion, the position which eliminates any tendency for separation of the two bones. This should also be kept in mind in cases in which there is a posterior marginal fracture of the tibia, as the usual position of fixation in dorsiflexion may at the same time cause separation of the fibula from the tibia.

In certain cases of diastasis associated with Pott's fracture and posterior tibial marginal fracture in which the fibula is broken two or three inches above the ankle joint, Gatellier's [3] approach has been found to be very satisfactory. This method is used when, for some reason or other, the posterior tibial fragment cannot be brought down into normal position. A lateral peroneal approach is made and the peroneal tendon retracted forward. The distal end of the fibula is freed and reflected downward, the external lateral ligaments acting as a hinge. The posterior tibial fragment is accurately reduced and fixed with screws. The fibula is then replaced and fixed with screws and the peroneal tendons are brought back into their normal positions.

3445 Prytania Street.

3. Gatellier, Jean: The Juxtaretroperoneal Route in the Operative Treatment of Fracture of the Malleolus with Posterior Marginal Fracture, Surg., Gynec. & Obst. **52**: 67-70, 1931.

ABSTRACT OF DISCUSSION

DR. CLAY RAY MURRAY, New York: Dr. Alldredge's paper has presented clearly a frequent problem in ankle fractures which is often overlooked with resultant disability. Disruption of the inferior tibiofibular joint is a common complication of high fractures of the lower fibula and a frequent enough complication of other ankle fractures. It is usually a far more serious lesion than any of the associated fractures from the standpoint of difficulty of treatment as well as resultant disability. Treatment of it does not enter into consideration in many cases because its presence is not recognized. Often the discovery of a widened mortise, an unstable ankle and a secondarily stiff and painful joint due to traumatic arthritis is made in a follow-up examination many months after the original injury. He has outlined clearly the important points in the diagnosis of this condition. It should be looked for and eliminated as a possibility in all ankle fractures before treatment for the fracture is instituted. Its common occurrence is one of the best arguments I know of against the marked inversion of the foot so commonly practiced in the immobilization of ankle fractures, since it is with marked inversion or eversion of the foot that x-ray examination most clearly demonstrates the diastasis of the tibiofibular joint. With proper x-ray examination using, as Dr. Alldredge suggests, a position (among others) which gives an anteroposterior view of the ankle with the foot in eversion or pronation (Dr. Alldredge refers to it as external rotation), the diastasis when present can be clearly shown. Marked inversion or supination of the foot will produce the same result. It is obvious then that any marked eversion or inversion of the foot as a position of fixation is a sure way to maintain the diastasis. When reduction is delayed in these cases, clotting of hemorrhage and exudate in the widened joint space may prevent reduction by closed methods, and interposition of ligamentous tissue or bone fragments may have the same effect. Failure to correct the diastasis is revealed in the postreduction x-ray films if they are taken in accordance with the directions given in Dr. Alldredge's paper. In the event of such failure, operative measures are indicated. When no such interposition exists, which is in the majority of cases, the reduction must, in addition to replacing bone fragments, firmly compress tibia against fibula at the tibiofibular joint, and the fixation must maintain this compression not only until such time as the ligaments have healed but until the healing has become strong enough to stand the strain of dorsiflexion of the foot. Where the diastasis has been rather easily recognized, full weight bearing on these ankles, even though the x-ray films may appear perfectly satisfactory, should be delayed for from twelve to sixteen weeks from the time of injury.

DR. GEORGE O. EATON, Baltimore: Dr. Alldredge is to be congratulated on emphasizing the presence and the importance of a tibiofibular diastasis. There is one point that I feel like complaining about. Dr. Alldredge states that fluoroscopic examination of the ankle is probably not as accurate as x-ray films. I think this is an understatement of fact. I think it is a deplorable habit to depend on fluoroscopic examinations as the x-ray diagnosis of fractures. If a fracture is present one should have x-ray films not only as a permanent record but also as a guide in attacking the problem of reducing the fracture. If the injury to the ankle is a fracture or a fracture without displacement, more often than not it will be missed if dependence is placed on fluoroscopic examination. As regards the posterior tibial marginal fracture, by far the majority of these marginal fractures are less than 30 per cent of the tibial plafond, and conservative treatment in addition to the reduction of the other fractures present can be depended on to yield a good result. Dr. Alldredge's paper is certainly excellent and timely and the literature, as he stated, is scarce on this important subject.

DR. RUFUS H. ALLDREDGE, New Orleans: I tried to stress the treatment of these ankle joint injuries with especial reference to the normal physiologic motions of the fibula. I have also tried to summarize the diagnostic points. As far as the use of the fluoroscope is concerned, in contrast to examination of

carefully taken x-ray films, I can only say that I think in most cases one can make a diagnosis from the x-ray film if one knows what to look for in the way of abnormalities. In posterior marginal fracture of the tibia, unless it is large enough to cause disturbance in function later or unless it is associated with fracture of the lower third of the fibula, together with rupture of the tibiofibular ligaments, it is not necessary to use the radical approach as it can be exposed simply through a posterior incision on the medial aspect of the achilles tendon.

MILKERS' NODULES

FREDERIC T. BECKER, M.D.
DULUTH, MINN.

The opportunity to observe and study four cases of milkers' nodules during the summer of 1939, and my inability to find in the American literature any description of this disease, prompt this report. This is an occupational infection of milkers which may be widely distributed among the dairying communities of our country. Is is my purpose to give a clinical description of milkers' nodules and differentiate this disorder from other diseases occurring on the hands of milkers, and discuss the cause, pathology and immunology.

The initial lesions may vary from one to forty in number and they are usually located on the hands and fingers. The incubation period is from five to seven days after contact with a diseased cow, and the infection enters the human skin through abrasions. At the onset an erythematous papule develops, which slowly increases in size, becoming a firm, elastic, bluish red nodule from 1 to 2 cm. in diameter. The lesions may be surrounded by an inflammatory areola and may be found in various stages of development. The nodule becomes semiglobular with a central depression; the surface becomes flat, and when the grayish loose epidermal covering is removed a reddened, granulating base remains. The nodule itself gives rise to few subjective symptoms, only slight pain and mild itching. As healing progresses the entire nodule flattens and the granulation tissue is absorbed; involution becomes complete in from four to six weeks without scar formation. The regional glands are occasionally enlarged and secondary pyogenic infection with lymphangitis may occur. There is little constitutional reaction except in unusual instances, when the eruption becomes generalized or secondary infection ensues.

According to Kummer [1] there have been twelve reports in which a generalized eruption has occurred. These disseminated lesions are multiform in type, being either umbilicated papules, urticarial wheals or macules, any of which may become vesicular or hemorrhagic. This generalized outbreak subsides within a week, and the eruption has been considered as being either toxic or produced by hematogenous dissemination of the infection.

All cases of milkers' nodules have occurred in people employed as milkers of cows on whose udders crusted or ulcerated lesions were found to be present. All cases have developed in the latter part of the summer. One attack apparently leaves immunity, since we have been unable to ascertain any instance of a recurrence. Most veterinarians have diagnosed the lesions which were present on the cows as being similar to those of cowpox.

DIFFERENTIAL DIAGNOSIS

European investigators differentiate milkers' nodules from other conditions many of which would seldom offer confusion in this country. Symmetrical tyloma of Arzt [2] consists of bilateral calluses located on the knuckles of both thumbs in persons using the Swiss method of milking. Jadassohn [3] described inflammatory nodules which are produced by cow hair entering calluses or fissures. Continental authors also consider hoof and mouth disease in differentiation, but the absence of oral lesions and systemic reaction in milkers' nodules should be sufficient to avoid confusion. In exceptional cases, when the eruption becomes generalized, erythema multiforme might be considered. I considered pyogenic granuloma when I saw my first case, but history of contact with an infected cow, the spontaneous resolution of the nodule, and microscopic examination were diagnostic criteria. The relation to vaccinia will be discussed with the consideration of the cause.

ETIOLOGY AND REVIEW OF THE LITERATURE

The majority of investigators think a virus is the infectious agent. Its relation to cowpox has led to much controversy. Winternitz,[4] who described the first case of milkers' nodules in 1899, was uncertain about the cause. Frieboes [5] in 1914 reported a case and inoculated the material into a scarified rabbit's cornea with negative results. He supported cowpox as the cause because the cattle which had been the source of the infection were considered to have this disease by the veterinarians. Paschen [6] made an extensive review of the literature and was of the opinion that cowpox and milkers' nodules could be sharply separated. He stated that in a disease caused by a pox virus a positive Paul's [7] test [8] should be obtained and in all individuals who were infected, either human beings or experimental animals, should be immune to later vaccination with vaccine virus. He was unable to come to any definite conclusion but suggested that the disease was a result of an infection of milkers with vaccine virus which was attenuated by a secondary invader.

Schultze, Seifried, and Schaaf [9] were among the first investigators able to demonstrate experimentally any relation to vaccinia. They studied twenty cases in various stages of development and by inoculating material from the nodules into calves were able to produce lesions similar to cowpox. Their experimental animals as well as the human patients proved resistant to vaccination with cowpox and reinoculation with a filtrate from

From the Duluth Clinic.

Read before the Section on Dermatology and Syphilology at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. Kummer, L.: Melkerknoten, in Arzt, Leopold, and Zieler, Karl: Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1934, pts. 11-12, vol. 3.

2. Arzt, Leopold: Ueber Berufserkrankungen bei Melkern, Wien. klin. Wchnschr. **37**: 630, 1924.

3. Jadassohn, Josef, cited by Paschen.[6]

4. Winternitz, R.: Knotenbildungen bei Melkerinnen, Arch. f. Dermat. u. Syph. **49**: 195, 1899.

5. Frieboes, W.: Ueber sogenannte Melkerknoten, Dermat. Ztschr. **21**: 310, 1914.

6. Paschen, Ernst: Melkerknoten, in Jadassohn, Josef: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2, p. 251.

7. Paschen, Ernst: Der Paulsche Versuch, in Jadassohn, Josef: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2, p. 169.

8. Paul found that material from lesions of smallpox and vaccinia when inoculated into a rabbit's cornea produced a keratitis which was plainly visible when the eye was immersed in sublimated alcohol. Microscopic sections of this material revealed gram-negative inclusion bodies (Guarnieri) in the epithelial cells.

9. Schultze, W.; Seifried, O., and Schaaf, J.: Die Melkerknoten und ihre Aetiologie, Ztschr. f. Infektionskr. d. Haustiere **31**: 295, 1927.

milkers' nodules. These workers also obtained positive Paul's tests in which they demonstrated Guarnieri bodies and they believed that the repeated trauma associated with the occupation of milking favored the development of nodules in some persons rather than the typical vesicopustules of vaccinia.

Stark and his co-workers [10] published an account of experimental and clinical investigation of an epidemic occurring in packing house workers who handled sheep. After repeated animal transfers they were able to produce pox lesions in which they could demonstrate inclusion bodies. These authors believed that their observations spoke for the identity of the virus of milkers' nodules with that of variola vaccine, the former undergoing alteration in its biologic properties by parasitism in foreign hosts, the original properties being recovered by repeated animal transfers.

Gottron [11] vaccinated a cow with material from a nodule and produced a papulopustular eruption which was indistinguishable from cowpox; however, he obtained a reinfection in the same animal with pox virus eight weeks later. Tappeiner [12] in his case obtained a positive Paul's test in which Guarnieri bodies could be demonstrated, but the reaction took five days instead of the usual two. He and Gottron were of the opinion that the virus of milkers' nodules was less virulent than that of cowpox.

Many of the recent workers have considered the paravaccine of Lipschutz [13] as the etiologic agent. Lipschutz found that some people when vaccinated develop a dark red papule instead of the usual vesicopustular reaction. In these lesions he was able to find gram negative inclusion bodies. The infection could be transmitted to animals and human beings but those infected showed no immunity to vaccinia. He also found the virus both of vaccinia and of paravaccinia present in the same calf lymph; the latter, however, did not produce a positive Paul reaction. The microscopic and immunologic studies in paravaccinia as described by Lipschutz resemble those found in milkers' nodules.

Dolgov and Morosov,[14] Zenin,[15] Falchi [16] and Bonnevie,[17] after reviewing the literature and studying their cases, considered the cause of milkers' nodules to be a virus similar to variola vaccine and believe "paravaccine of Lipschutz" the most likely. They based their conclusion on the variation in the pathology of variola and milkers' nodules, the lack of immunity to vaccination with cowpox, and the absence of pustulation in milkers' nodules, which healed spontaneously without scar formation.

Groth,[18] Kaiser and Gherardini [19] and Woringer [20] stated that they were unable to make any definite conclusions as the result of their observations, but they found little evidence to favor vaccine virus as a cause of milkers' nodules.

Histologic interpretations of biopsy specimens of milkers' nodules depend on the age of the lesions. Schultze, Seifried and Schaaf, Woringer and Bonnevie found that in an early lesion there was acanthosis and reticular degeneration [21] of the upper cells of the malpighian layer with formation of microscopic multilocular vesicles. Considerable edema of the papillae and corium developed with vascular and lymph vessel dilatation accompanied by an infiltration with various cells, of which eosinophils were prominent. Later parakeratosis and hyperkeratosis were present and in the corium granulation tissue developed. Bonnevie found that the histologic changes in upper layers of the epidermis resembled the reticular degenerative changes seen in variola except that the multilocular vesicles that were formed in milkers' nodules remain microscopic. The hyperkeratosis present probably prevented the vesicles from becoming larger or reaching the surface. The exudate in the epidermal vesicles of milkers' nodules however, in contrast to variola, does not become pustular, and the dermis of the nodules is characterized by the formation of granulation tissue.

Fig. 1 (case 2).—Typical milkers' nodule with two secondary lesions. Photographed by Dr. R. H. Puumala.

REPORT OF CASES

CASE 1.—S. N., a white youth aged 16 years, had never been vaccinated for smallpox. He spent his summer vacation on a farm, where he milked cows that had "crusted sores" on their udders. A small dark red pea sized papule developed between the first and second fingers of the right hand. The lesion slowly grew larger until it became the size of a cherry. At the end of three weeks he consulted his local physician, who described the lesion as a semisolid brownish red nodule 1 cm. in diameter which was covered by a dried grayish epidermis, which he easily removed. The patient was referred to me and examination showed a nodule 0.75 cm. in diameter of red granulation tissue. One right axillary gland was enlarged to the size of a walnut and was slightly tender. My first diagnostic impression was pyogenic granuloma. However, the unusual history of contact with sores on cattle prompted the performance of a biopsy, after which the remainder of the nodule was cauterized. Healing was uneventful and took place

10. Stark, A. M.: Tiesenhausen, M. M.; Gožanskaja, N. M.; Skrozky, E. W., and Schtschastny, D. S.: Ueber die Pockenätiologie der sogenannten Melkerknoten, Arch. f. Dermat. u. Syph. **170:** 38, 1934.

11. Gottron, Heinrich: Beitrag zur Aetiologie de Melkerknoten, Dermat. Ztschr. **58:** 207 (May) 1930.

12. Tappeiner, Sepp: Zur Frage der vakzinalen Aetiologie der Melkerknoten, Wien. klin. Wchnschr. **51:** 1061 (Sept. 23) 1938.

13. Lipschutz, B.; Paravaccine, in Jadassohn, Josef: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2, p. 80.

14. Dolgov, A., and Morosov, M.: Zur Frage der Aetiologie der Melkerknoten, Sovet. vestnik Dermat. **9:** 338, 1931.

15. Zenin, A. S.: Beitrag zur Kenntnis der sogenannten "Melkerknoten," Dermat. Wchnschr. **94:** 605 (April 30) 1932.

16. Falchi, Giorgio: Rilievi clinici e ricerche sperimentali sui noduli vaccinali, Gior. ital. di dermat. e sif. **77:** 181 (April) 1936.

17. Bonnevie, Paul: "Milkers' Warts": Infection from "False Cowpox," with Paravaccinal Virus, Brit. J. Dermat. **49:** 164 (April) 1937.

18. Groth, A.: Zur Aetiologie der Melkerknoten, München. med. Wchnschr. **76:** 2128 (Dec. 20) 1929.

19. Kaiser, M., and Gherardini, Maria: Studien über Melkerknoten, Arch. f. Dermat. u. Syph. **169:** 77, 1933.

20. Woringer, F.: Deux nouveaux cas de tubercules du trayeur, Bull. Soc. franç. de dermat. et syph. (Réunion dermat.) **41:** 197 (Feb.) 1934.

21. Unna (Die Histopathologie der Hautkrankheiten, Berlin, A. Hirschwald, 1894) described reticular degeneration as a vacuolar deterioration of the cells of the upper rete malpighii producing large clear cells in which some of the cellular membranes rupture, producing multilocular vesicles.

within ten days. The patient was vaccinated two weeks after the lesion healed; a positive reaction developed which produced a typical scar.

Case 2.—J. H., a patient of Dr. R. H. Puumala of Cloquet, Minn., a white youth aged 18 years, was never vaccinated and had milked cows on his father's farm for the past nine years.

Fig. 2.—Low power magnification of section from case 2 showing hyperkeratosis, multilocular vesicles and dense cellular infiltrate in the dermis; stained with hematoxylin-eosin.

In June 1939 he first noticed that some of the cows developed crusts on their udders. About the middle of August a small papule developed at the site of a scratch on the medial surface of the first finger of the left hand; this lesion slowly grew larger and four days later two others started on the dorsolateral aspect of the right wrist and thumb. My examination on August 28 showed a hard, nonpainful, brownish red nodule on the left index finger, 1 cm. in diameter and 4 mm. high. The top surface was slightly delled. The lesions on the right hand were pea sized papules with a small central vesicle. Both right and left epitrochlear glands were enlarged to about the size of a hazelnut and two axillary glands were the size of a walnut and slightly tender. A punch biopsy was taken of the first lesion on the left index finger. Half of the material was emulsified and some of it was instilled into the scarified cornea of two rabbits and the rest was injected into the skin and foot pads of two guinea pigs. The other half was placed in solution of formaldehyde, embedded in paraffin, sectioned and stained with hematoxylin and eosin. All lesions were dressed with sterile petrolatum and observed every other day by Dr. Puumala, who reported that the lesions were entirely healed in one month without any scar except at the site of the biopsy wound. At this time he vaccinated the patient with smallpox vaccine, which produced a positive reaction that resulted in the classic scar.

Case 3.[22]—Mrs. M. W., a white woman aged 27, seen Sept. 1, 1939, milked cows at irregular intervals during the past year and stated that one of the animals had sores about the udder. Three weeks previous to the time of consultation she noticed a lesion on the right thumb which continued to grow. Examination showed a round, bluish red button-like tumor 1.5 cm. in diameter on the first joint of the right thumb. The center was slightly depressed and whitish. There were no palpable enlarged lymph nodes. The nodule was removed and divided in half; one portion was fixed in solution of formaldehyde and sectioned and stained with hematoxylin and eosin. The other part was emulsified and some of it instilled in the scarified cornea of a rabbit and the rest injected into the thigh and skin of two guinea pigs.

Case 4.—Mrs. L. W., a farmer's wife aged 28, observed Sept. 29, 1939, stated that she developed about three weeks previously an eruption on the right little finger. Examination revealed an elevated bluish red semisolid tumor 1 cm. in diameter on the right little finger. The top surface of the growth was easily removed, leaving a red granulating surface. A biopsy was taken and the lesion cauterized, after which uneventful healing took place.

22. Cases 3 and 4 were observed by Dr. Stephen Epstein of Marshfield, Wis., and are recorded with his permission. The biopsy material was studied by me.

EXPERIMENTAL RESULTS

The corneas of all rabbits inoculated with material in cases 2 and 3 were watched daily for a period of two weeks and no reaction took place and the corneas remained clear. The guinea pigs were kept under observation for two months. No inflammatory reaction occurred at the injection sites. They were killed at this time and no evidence of any infection could be found at pathologic examination. Cultures were made on all types of routine mediums with the emulsified material from cases 2 and 3 and no growth was obtained.

HISTOLOGY

The microscopic examinations in my four cases were similar to those described in the literature and the essential features which I found may be summarized as follows:

There was considerable increase in the stratum corneum with hyperkeratosis and parakeratosis (fig. 2). Acanthosis and spongiosis were present and in the upper layers of the rete malpighii there was an increased intracellular edema which produced in some scattered

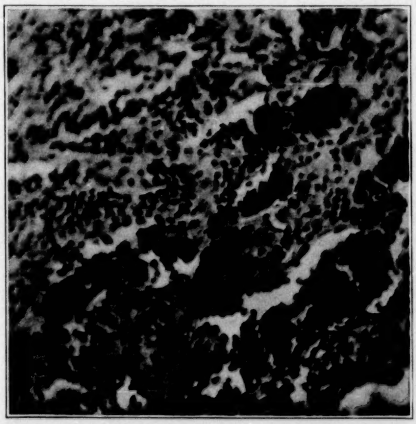

Fig. 3.—High power reproduction of figure 2, showing the dermis with dense multicellular infiltrate and marked blood vessel dilatation.

areas enlarged clear cells with only a thin cellular membrane and in other areas there were microscopic multilocular vesicles. The dermis was edematous with an increased vascularity (fig. 3) and dense cellular infiltration was present which disrupted the epidermal-dermal junction. This infiltrate was made up principally of

lymphocytes and also many plasma cells, eosinophils and an occasional giant cell and polymorphonuclear leukocyte. The increased intracellular edema with the formation of microscopic multilocular vesicles could be interpreted as a mild degree of reticular degeneration as described by Unna. In none of the microscopic sections studied was there any evidence of pustulation.

COMMENT

It is quite evident both clinically and histologically that the lesions occurring in the four cases described are similar in nature to those recorded in the German literature as "melkerknoten." All individuals afflicted had been engaged in milking cows on whose udders open ulcers or crusted lesions had been present. The cause of milkers' nodules is undoubtedly infectious, because the condition is self limited, healing spontaneously without treatment and apparently leaving an immunity to further similar inoculations. My inability to demonstrate any bacteria both by culture and by animal inoculation, plus the fact that many investigators have found inclusion bodies in a microscopic section, would indicate that the infecting agent is a filtrable virus.

The relation of this virus to vaccinia is still in a controversial state. The first to show any definite relation between the two were Schultze, Seifried and Schaaf. Paschen and Groth, however, believed that these cases were vaccinia and not true milkers' nodules. Experimental work of Stark and his co-workers supported the theory that the organism of milkers' nodules was of decreased virulence because only after repeated transfers to the same species of animals were they able to show conclusive evidence that the virus had the characteristics of variola vaccine.

It is generally agreed that for a virus to be similar to that of variola a positive Paul test must be obtained and the individual infected should acquire an immunity against vaccine virus. The majority of investigators of milkers' nodules have been unable to obtain positive Paul reactions from their cases and most of their patients have not acquired any immunity to smallpox vaccine. My results of a negative Paul test in two of the cases and a lack of immunity to vaccination as demonstrated in two others agrees with most authors. Therefore, because of these two facts along with the difference in the histologic picture and in the clinical course of milkers' nodules there does not seem to be much evidence to support any relation to variola vaccine. On the other hand, the pathologic process of milkers' nodules seems to show a close similarity to paravaccinia, as neither of the disorders produces immunity to subsequent inoculation with vaccine virus, the Paul test is negative and the microscopic appearances are similar in the two instances.

SUMMARY

1. Four cases of milkers' nodules, which is an infection of human beings acquired by milking diseased cows, were observed.

2. No relation between milkers' nodules and vaccinia could be demonstrated in these cases, as the Paul test, which was performed with material from two cases, was negative and two of the infected persons showed no immunity to smallpox vaccination.

3. The clinical course of milkers' nodules and the distinct variations in the pathologic picture are further evidences that this disease shows no relation to variola vaccine.

4. The cause of milkers' nodules is apparently a virus, which may be either an attenuated or biologic modification of vaccine virus. From all evidence it more closely resembles the paravaccine of Lipschutz.

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ABSTRACT OF DISCUSSION

DR. M. E. OBERMAYER, Chicago: Dr. Becker's presentation is thorough and complete, and it answers a long-felt need. In the United States, large sections of which are agricultural, an occupational disease among milkers is bound to be far more widespread than is indicated by the scarcity of case reports. There is still a great deal of controversy concerning the etiologic agents of the disorder. The only point on which the various investigators agree is that the condition is undoubtedly caused by a filtrable virus. In regard to the nature of the virus there are three schools of thought: (1) that the virus of milkers' nodules is identical with that of vaccinia, (2) that the virus of milkers' nodules represents an attentuated or biologically modified vaccinia virus or (3) that the virus of milkers' nodules has nothing to do with that of vaccinia but is identical with the virus of paravaccinia of Lipschütz. From what Dr. Becker said and from some additional references it seems that the evidence gathered for each of the three points of view is sufficiently strong to substantiate the choice of virus assumed to be responsible in each particular case which was studied. If to prove the identity of the virus of milkers' nodules with that of vaccinia three criteria must be met, namely (*a*) a positive Paul test, (*b*) demonstration of Guarnieri bodies and (*c*) failure to produce a positive take in the patient by ordinary antismallpox vaccination, satisfactory proof has been obtained though only in a small number of instances. The second assumption, that the virus represents an attenuated or biologically modified vaccinia virus, has been substantiated by the properties which the virus has exhibited after repeated animal transfers. The results of Dr. Becker's study led him to conclude that the third theory about the etiologic agent, supported by the evidence from his own cases, is the most acceptable. When reviewing the experimental data critically, I feel that the evidence which has been presented in favor of each of the three suggestions need not necessarily be considered conflicting if it is assumed that milkers' nodules represent a clinical entity caused by filtrable viruses of different kinds. The disorder may be caused at times by the ordinary virus of vaccinia, more often by an attenuated or biologically altered vaccinia virus and frequently by the virus of paravaccinia. The fact that the viruses of vaccinia and of paravaccinia have been found simultaneously in the same lymph is suggestive. Moreover, there seems to be evidence that the clinical aspects of the disease on the udders of the animals are not uniform. Thus the assumption of multiple etiologic agents of the disorder seems to me a logical means of bringing the seemingly conflicting evidence into agreement.

DR. C. GUY LANE, Boston: This condition is relatively unusual. The photograph which was shown on the screen was made last fall of these two lesions of three weeks' duration. The lesions presented themselves within two or three days after this man started working on a farm milking cows. He had not done this work for some twenty years previously. He noticed small erosions first, at the sites of friction between his fore and middle fingers following the beginning of his new job of milking. Then there was gradual development at the sites of the lesions which were shown on the screen. There were vesicles at the start, blisters that became eroded and then gradually became elevated. In one axilla there were one or two palpable tender glands. Our cultures at the hospital showed only staphylococci. The interpretation of the biopsy was at that time simply chronic inflammatory reaction. There is nothing known in this particular case with reference to the condition of the cow. The lesion subsided relatively readily under mild antiseptic therapy. It is interesting to review these cases and analyze our reasons for deciding that these are occupational. In the first place they occur so far as we know only in the agricultural occupations, those having to do with animals. The lesions are consistent with those which have previously been described in the literature.

The time relationship is correct since this condition appears relatively few days after the patient has begun the job. Again, their site of onset is the site of the maximum trauma, or the site of the particular trauma, where greatest friction occurs, and as far as is known at present there is no other known source of this infection.

DR. FREDERIC T. BECKER, Duluth, Minn.: From the contact I have had in the Scientific Exhibit, I am sure that milkers' nodules are not rare in this country. Many doctors who are located in dairying communities have seen these cases at intervals. I think that calling attention to it will bring forth many new cases.

TROPHIC LESIONS IN THE DISTRIBUTION OF THE TRIGEMINAL NERVE

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AND
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To the neurologist, bona fide trophic changes are lesions appearing in tissues which have been deprived of certain qualities of sensation, particularly those of pain and temperature.

That portion of the face which is supplied by the trigeminal nerve may be thus denervated by a number of organic disturbances. The neurosurgeon accomplishes this by sectioning the nerve through its peripheral branches, the gasserian ganglion, the posterior root or, more selectively, by the newest procedure devised by Sjöqvist,[1] namely cutting the descending spinal tract in the medulla.

Occasionally a tumor or an inflammatory process may be so peculiarly situated near the ganglion or in the brain stem as to interrupt the sensory function and cause some degree of anesthesia in the face. Most striking is the analgesia produced by two well known lesions of the medulla, namely occlusion of the posterior inferior cerebellar artery and syringobulbia.

The whole subject of trigeminal nerve function has undergone a recent renaissance and a wealth of literature has emerged, representative of which are the studies of Sjöqvist;[1] Walker;[2] Rowbotham;[3] Smyth[4] and Lewy, Groff and Grant.[5] In all these discourses little is said of neurotrophic lesions in the trigeminal area for the reason that such disturbances are rather rare. This, of course, is true only if one excludes the simple herpetic eruptions about the lips which occur in many febrile diseases and if one also makes an exception of the corneal complications following section of the trigeminal nerve. The more malignant herpes which is associated with persistent neuralgia is of uncommon occurrence. Peet[6] found only three cases among 400 sufferers with facial neuralgia and quoted Frazier as having encountered but one instance in 520 cases, while Cushing mentioned herpetic neuralgia in only three of 332 operations on the gasserian ganglion.

This discussion concerns itself with trophic lesions which are nonherpetic in nature. The three examples which are presented have all been studied by competent dermatologists, who found no explanation for the appearance of the lesions except on a neurotrophic basis. These cutaneous phenomena have these features in common: They are implanted on areas definitely devoid of pain and temperature sense and they all conform sharply to neuroanatomic delineations. They differ in that the interruption of sensation occurs at different levels in the trigeminal system: In the first case the changes in the skin followed a gasserian section, in the second case it is clinically assumed that the disturbance was caused by an occlusion of the posterior inferior cerebellar artery, and in the third case the symptoms were typical of syringobulbia.

DERMATITIS FOLLOWING GASSERIAN SECTION

Simple erythematous eruptions following trigeminal nerve section are unusual, unpredictable and puzzling phenomena. In a review of 107 cases in which the ganglion or the posterior root was cut, Becker[7] was able to find only five cases in which cutaneous manifestations were presented. He himself reported the case of a 47 year old woman who developed an erythematovesicular eruption, which appeared three weeks after an operation for trigeminal neuralgia.

The following case, of a cutaneous disturbance previously reported by Netherton[8] from the point of view of a dermatologist, is now reviewed after further study of the process and its relation to the neural defect:

CASE 1.—A woman aged 44 came to the Cleveland Clinic in March 1930 for relief from paroxysmal facial neuralgia, characterized by a hot, jagging pain over the left side of about five years' duration. The attacks were induced by rubbing the upper or lower eyelid and by talking or chewing.

Nothing of significance was elicited from her history except that she had occasional attacks of urticaria and a mild eczema had developed in the flexor regions of the extremities.

Surgical treatment consisted of a total section of the first and second divisions and a partial section of the third division of the trigeminal nerve. A year later an erythematous plaque developed on the left side of the forehead, to be quickly followed by similar lesions over the left temple, the lower lip, the left cheek and the left side of the nose. The areas gradually became confluent, and a sharp line of demarcation between normal and abnormal skin developed in the middle of the face. The erythematous flush was particularly prominent in the areas supplied by the first and second divisions of the severed trigeminal nerve and faded diffusely into the zone of the third division.

Neurologic examination disclosed marked hypesthesia to all qualities of sensation in the areas supplied by the ophthalmic and mandibular divisions and total anesthesia in the area assigned to the second division. There was typical absence of the corneal reflex on the affected side, but no evidence of involvement of the sympathetic nerves. Thermocouple readings were similar on the two sides of the face.

The cutaneous disturbance remained strictly unilateral in distribution. It was not accompanied by pain or other subjective disturbances. There was no induration of the underlying tissues. Exposure to cold, heat, wind, soap and water produced periodic exacerbations of an exudative inflammation, followed by increased desquamation.

Read before the Section on Nervous and Mental Diseases at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

From the Division of Neuropsychiatry, Cleveland City Hospital, and the Department of Nervous and Mental Diseases, Western Reserve University School of Medicine (Dr. Karnosh).

1. Sjöqvist, O.: Studies on Pain Conduction in the Trigeminal Nerve, Acta psychiat. et neurol. (supp.) **17**: 1-139, 1938.

2. Walker, A. Earl: Anatomy, Physiology and Surgical Considerations of the Spinal Tract of the Trigeminal Nerve, J. Neurophysiol. **2**: 234-248 (May) 1939.

3. Rowbotham, G. F.: Observations on the Effects of Trigeminal Denervation, Brain **62**: 364-380 (Dec.) 1939.

4. Smyth, G. E.: The Systemization and Central Connections of the Spinal Tract and Nucleus of the Trigeminal Nerve: A Clinical and Pathological Study, Brain **62**: 41-87 (March) 1939.

5. Lewy, F. H.; Groff, R. A., and Grant, F. C.: Autonomic Innervation of the Eyelids and the Marcus Gunn Phenomenon, Arch. Neurol. & Psychiat. **37**: 1289-1297 (June) 1937.

6. Peet, M. M.: Postherpetic Trigeminal Neuralgia: Persistence of Pain After Section of the Sensory Root of the Gasserian Ganglion, J. A. M. A. **92**: 1503-1505 (May 4) 1929.

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8. Netherton, E. W.: Persistent Dermatitis: Unusual Sequela of Radical Operation for Trigeminal Neuralgia, J. A. M. A. **100**: 722-724 (March 11) 1933.

All this embarrassed the patient greatly and handicapped her in business. She managed a meat stall in a large open market. Would-be customers glanced at her facial blemish and passed on to trade with her competitors. Despite various topical applications, the condition remains essentially unimproved at the present time. Biopsy of the skin was not allowed.

In attempting to explain the relation of eczema to nerve injury such as is here presented, dermatologists can offer only an empiric opinion. Bruck [9] expressed the belief that many skin eruptions of this nature may be of true neural origin, but only when the damage is limited to the somatic sensory fibers while the sympathetic and vasomotor mechanisms are intact. Such an explanation, however, is inadequate, for this very situation obtains in almost every case of neuralgia following trigeminal nerve section and yet eczema rarely follows. The preexisting allergy may be significant, and the singular disposition to eczema in other parts of the body must be considered as a factor in determining this unusual reaction to facial hemianesthesia.

TROPHIC CHANGES FOLLOWING THROMBOSIS OF THE POSTERIOR INFERIOR CEREBELLAR ARTERY

Bruck's theory is even less tenable in explaining trophic changes which occur on the face after an occlusion of the posterior inferior cerebellar artery, for not only is there marked analgesia of the homolateral

Fig. 1 (case 2).—Appearance of lesions.

side of the face but the sympathetic and vasomotor fibers are frequently involved in the same destructive process. Irrespective of the damage to the vegetative nerve components, the cutaneous changes may become extensive and pernicious and may cause severe distortion of the tissues of the face.

9. Bruck, C.: Nervenschädigung und Eksem: Ein klinischer Beitrag zur Frage der Eksempathogenese, Dermat. Ztschr. **55**: 7-13 (Dec.) 1929.

CASE 2.—A white man aged 48, a glazier, was suffering with diabetes, which was well controlled by 5 units of insulin before each meal. On the morning of Nov. 9, 1934, he was awakened by a peculiar sensation of numbness over the entire left side of the face and a deep, gnawing, burning pain about the left eye. On rubbing his face he found the right side to be moist with perspiration and the left side utterly dry. On

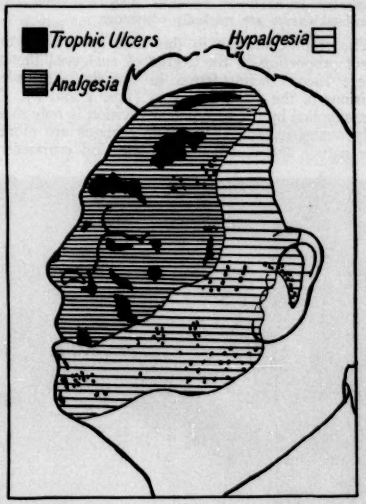

Fig. 2 (case 2).—Distribution of trophic lesions and of analgesia due to vascular softening of the lateral portion of the medulla following an occlusion of the posterior inferior cerebellar artery. Both ulceration and analgesia conform to the peripheral orientation of the trigeminal nerve. The area supplied by the geniculate portion of the facial nerve is spared.

attaining the sitting position in bed he became very dizzy and on attempting to stand he swayed strongly to the left.

The neurologic components of significance were as follows: The pupils were unequal, the left being very small and reacting slightly to the flashlight. There was a clockwise rotatory nystagmus when the gaze was directed to the left. The left corneal reflex was absent. The greater portion of the left trigeminal area was analgesic, while tactile sense was only moderately impaired. The sensory defect was pronounced in those areas in which the patient experienced the deep pain; that is, at the root of the nose and just under the left eye. The left side of the palate was poorly elevated. Excursion of the vocal cords was symmetrical. The left abdominal and cremasteric reflexes were absent. In the Romberg test the patient swayed violently to the left side.

The ulcers appeared about six weeks after the onset of the illness as small red patches at the left angle of the mouth, under the left eye and on the left side of the nose. These were entirely painless and gradually spread, leaving in their wake a reddened, puffy, indurated, crusted skin, which broke down again and again until there was considerable deformity of the face. Lesions appeared in the scalp, anterior to the ear and on the chin but never outside the left trigeminal area. Biopsy of the skin demonstrated no specific disease.

These distressing cutaneous changes on the left side of the face were accompanied by a Horner syndrome. There was a marked difference in the temperature of the skin on the two sides of the face. The Minor starch and iodine test, according to the technic outlined by List and Peet,[10] demonstrated com-

10. List, C. F., and Peet, M. M.: Sweat Secretion in Man: I. Sweat Responses in Normal Persons, Arch. Neurol. & Psychiat. **39**: 1228-1237 (June) 1938.

plete paralysis of sweating on the left side. A resection of the inferior cervical ganglion was done with the hope that by further increasing the blood supply the cutaneous lesions would improve. The procedure merely served to increase the enophthalmos. To roentgen therapy the response was equally indifferent.

At the present time the trophic process has advanced into the eyeball, the cornea being cloudy and showing extensive vascularization in its lower segments. The conjunctiva and all periorbital tissues are markedly edematous.

The trophic disease in this case appears to be in direct proportion to the degree of analgesia, the most severe lesions being found in the first and second divisions of the trigeminal area (figs. 1 and 2). The skin supplied by the mandibular division is only moderately analgesic, and the trophic changes are minimal. The nature and distribution of the skin eruptions are

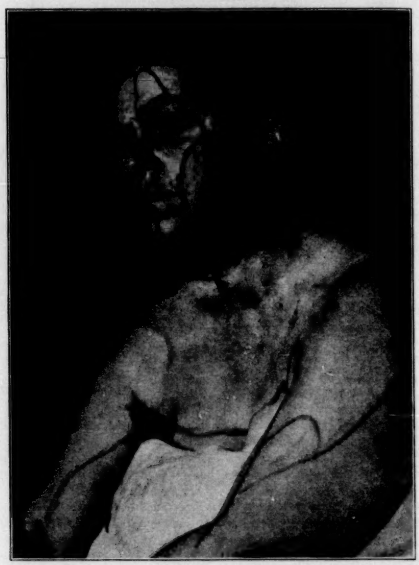

Fig. 3 (case 3).—Trophic ulcers and sensory defect in a case of syringobulbia.

in harmony with most of the descriptions of sensory change in the Wallenberg syndrome. Moreover, an identical sensory disturbance was found by Sjöqvist [1] and Walker [2] and by Grant, Groff and Lewy [11] in patients after tractotomy, so that one is fairly certain that this patient had a lesion in the descending spinal tract. Not only do the lesions orient themselves in their intensity according to the three peripheral divisions of the fifth nerve but both ulcerations and analgesia avoid the area assigned by Ramsay Hunt [12] to the sensory portion of the facial nerve. Whatever the pathologic process may be, this trophic change in a disease of the lateral portion of the medulla offers objective testimony that the descending spinal tract of the trigeminal nerve is fundamentally arranged to conform to the peripheral distribution of the nerve, a finding about which there is general agreement.

TROPHIC LESIONS IN SYRINGOBULBIA

No concerted opinion exists, however, with respect to the significance of the sensory changes which may occur in syringobulbia. Such tangible evidence of sensory loss as trophic ulceration of the face is usually wanting in this medullary disease. It is true that hyperostosis of the facial bones has been noted in syringobulbia, and in 1930 Thomas [13] described a case in which there was thickening of the left side of the face, but trophic changes in the skin itself are not mentioned in any clinical reports on this disease.

CASE 3.—A stocky white woman aged 37 first noticed numbness of the left hand and shoulder and the left side of the face five years before she came to the attention of the neurologic clinic at the City Hospital. The numbness of the face was more irritating than painful. She applied a heat lamp to the area, and quickly there developed shallow, painless ulcers about the left ear. These extended directly upward into the scalp and downward along the angle of the jaw.

The positive observations in the neurologic examination were as follows: The left corneal reflex was absent and there was a rotating type of nystagmus, more pronounced when the gaze was directed to the left. The gag reflex was absent on the left side, and the left vocal cord was inactive during phonation. The posture was stooped, with a thoracic kyphosis. There was slight atrophy of the muscles of both shoulder girdles, more marked on the right side. In the left hand the thenar eminence was small; in the right hand there was considerable atrophy of the interosseous tissues.

The sensory examination revealed anesthesia to pain and temperature on the left side of the head, limited anteriorly by a line passing from the vertex downward over the malar prominence to the angle of the jaw. This area of total analgesia extended backward into the scalp and downward over the neck and in mantle-like fashion over both shoulders to the elbows and the nipple levels of the chest. In the face, anterior to the analgesic zone, was a narrow band of hypalgesia, while the area about the nose, mouth and eye was essentially normal in pain and temperature sense. Tactile sense was well preserved everywhere, demonstrating the familiar dissociation of sense characteristic of syringomyelia. There was no involvement of the sympathetic nervous system.

The facial lesions appeared in the area which is supplied by overlapping branches of the trigeminal and the highest cervical nerves. The erosions spread, healed occasionally with a thick epithelial covering, only to reopen and increase in size. They eventually extended deep into the external auditory meatus. After many sporadic attempts at healing, a progressive induration ensued, leading to considerable cicatrization, particularly below the ear.

In this case the disposition of ulcers furnishes objective evidence of the peculiar nature of the sensory disturbances which occur in the trigeminal area in syringobulbia. Both the trophic ulceration and the sensory changes utterly ignore the peripheral orientation of the fifth nerve and dispose themselves in a segmental or concentric fashion converging on the nose and mouth (figs. 3 and 4). The erosions are equally heedless of the sensory architecture about the ear, involving the geniculate or facial components about the external auditory meatus and showing no regard for the peripheral topography of the auricular and occipital branches of the cervical plexus.

The concentric sensory zoning on the face is not an uncommon occurrence in syringobulbia and is observed

11. Grant, F. C.; Groff, R. A., and Lewy, F. H.: Section of the Descending Spinal Root of the Fifth Cranial Nerve, Arch. Neurol. & Psychiat. **43**: 498-509 (March) 1940.

12. Hunt, Ramsay: Geniculate Neuralgia (Neuralgia of the Nervus Facialis): A Further Contribution to the Sensory System of the Facial Nerve and Its Neurologic Conditions, Arch. Neurol. & Psychiat. **37**: 253-285 (Feb.) 1937.

13. Thomas, André: Forme unilatérale et sensitive de la syringomyélobulbie; coexistence d'apophyses cortiformes de la 7 cervicale, Presse méd. **38**: 611-612 (May) 1930.

in no other disease. Schlesinger [14] in 1895 and von Sölder [15] in 1899 noted that loss of pain sense first appeared in the scalp and advanced toward the nose and mouth. Dejerine [16] made the same observation and came to the conclusion that the trigeminal structures in the brain stem are segmentally arranged in terms of concentric circles converging on the nose. Woods [17] supported the same hypothesis after reporting two cases of syringobulbia. We investigated three cases of this disease and in only one was this type of sensory disturbance absent. Yet Taylor, Greenfield and Martin [18] and Jonesco-Sisesti [19] did not agree that this segmentation of pain sense is typical of syringobulbia. After making excellent clinicopathologic correlations, Smyth [4] ridiculed this concept of concentric zoning, although he conceded that it may be occasionally encountered. For this he had no explanation. Perhaps, as Sjöqvist suggested, this sensory disturbance is peculiar to syringobulbia because the disease primarily involves the second sensory neuron of the trigeminal nerve, the so-called quintothalamic tract. In its orderly ascent through the reticular portion of the brain stem the pathologic process exposed the segmental structure of this tract and its nucleus. It is conceivable that the irregular sensory disturbances observed by some writers are produced by a process which destroys parts of both the first and the second sensory neuron. Smyth admitted that the anatomic position of the quintothalamic tract is not clearly known, and his proof that it is not segmentally arranged is not very convincing.

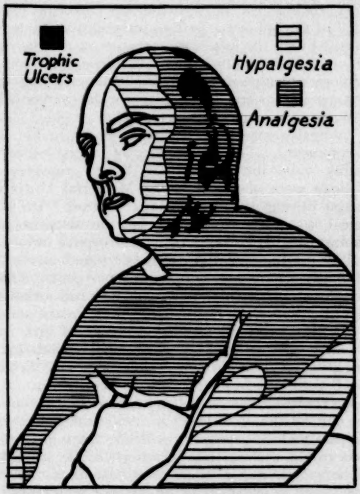

Fig. 4 (case 3).—Peripheral nerve topography is ignored, and the lesions of the skin as well as the analgesic areas are arranged in a concentric manner, with the zones converging on the nose and mouth.

In the case presented here the trophic erosions of the skin are so disposed as to support the theory that this tract conveying pain and temperature sensations across the medulla retains its primitive lamellar or segmental arrangement in the same manner as does its homologue in the spinal cord, namely the spinothalamic tract. That the latter structure, which is equally susceptible to syringomyelia, possesses this anatomic feature has been demonstrated in the clinical investigations of Tilney and Elsberg [20] and by the neurosurgical studies of Hyndman and Van Epps.[21]

SUMMARY

Neurotrophic changes in the trigeminal area of a nonherpetic type may occur in any disease which destroys the fibers conveying pain and temperature sense. That they are uncommon is probably due to the fact that the face is instinctively better protected from trauma than are other parts of the body which become analgesic. The erosive process on the skin can exist independent of sympathetic involvement. Skin eruptions of a trophic nature may arise as nonpredictable and embarrassing sequelae of nerve section for facial neuralgia.

Destructive lesions of the brain stem produce trophic disorders the distribution of which offers additional data as to the manner in which the fibers of the trigeminal pathways are arranged within the central nervous system. Vascular softenings which usually involve the lateral portions of the medulla produce sensory changes which conform to the peripheral distribution of the trigeminal nerve, while a process which primarily destroys the inner structures of the brain stem leads to analgesic areas with a concentric zoning converging on the nose and mouth.

ABSTRACT OF DISCUSSION

DR. MAX MINOR PEET, Ann Arbor, Mich.: I have no explanation for these trophic disturbances or diseases involving the trigeminal tract. I have seen three cases of apparent trophic disturbance in about 1,000 operations for section of the sensory root of the gasserian ganglion. Three tenths of 1 per cent is a very small incidence. In two of those cases there were rather marked paresthesias. This is a peculiar sensory disturbance when the face itself is absolutely anesthetic. The patient feels crawling or burning sensations and itching or tickling and more or less constantly traumatizes his face. One of these patients—and they all were elderly—constantly rubbed the nose or picked it, and I think possibly that was the cause of the disturbance. Both of these elderly persons who had this type of lesion had a slow, almost benign, ulceration starting in the ala of the nose, and it finally went to complete destruction of the lower corner of the ala and then extended slowly, gradually, over a number of years, out to the adjacent part of the cheek. The ulceration was exceedingly superficial. It would be healed much of the time and then break out again apparently under direct trauma. The patients both said they had these paresthesias, that they couldn't help picking at the nose or face, and they both thought this constant trauma was a factor. The third case developed in the ophthalmic division in the forehead. The patient came back several years after operation with typical whitish scars in the forehead, such as are seen after a true herpes, and I am not certain whether this patient actually developed a true herpetic lesion superimposed on an anesthetic area following section of the sensory root. In the last patient that had this destruc-

14. Schlesinger, H.: Die Syringomyelie, Leipzig, Franz Deuticke, 1895.

15. von Sölder, F.: Der segmentale Begrenzungstypus bei Hautanästhesien am Kopfe, inbesondere in Fällen von Syringomyélie, Jahrb. f. Psychiat. u. Neurol. **18**: 458-478, 1899.

16. Dejerine, J.: Sémiologie des affections du système nerveux, Paris, Masson & Cie, 1914, p. 800.

17. Woods, A. H.: Segmental Distribution of Spinal Root Nucleus of the Trigeminal Nerve, J. Nerv. & Ment. Dis. **110**: 91, 1913.

18. Taylor, J.; Greenfield, J. G., and Martin, J. P.: Syringomyelia and Syringobulbia, Brain **45**: 323-356 (Dec.) 1922.

19. Jonesco-Sisesti, N.: La syringobulbie: Contribution à la physiopathologie du tronc cérébrale, Paris, Masson & Cie, 1932.

20. Tilney, Frederick, and Elsberg, C. A.: Sensory Disturbances in Tumors of the Cervical Spinal Cord, Arch. Neurol. & Psychiat. **15**: 444-454 (April) 1926.

21. Hyndman, O. R., and Van Epps, Clarence: Possibility of Differential Section of the Spinothalamic Tract, Arch. Surg. **38**: 1036-1053 (June) 1939.

tion of the ala of the nose I had our dermatology department study the patient. There were no signs of malignancy. There were semicutaneous changes in other parts of the face and body and the dermatology department didn't want to say whether this was trophic, whether this was actually in any way related to section of the sensory root of the gasserian ganglion or whether it was a traumatic lesion incident to the paresthesia that the patient was suffering. It seems that, if we are going to assume that these are trophic, they ought to occur in a much higher percentage of cases. We know the very high incidence of herpes which occurs after operation. For a long time I assumed that these herpetic manifestations were due to injury directly to the gasserian ganglion incident to its exposure. I do not take up the ganglion, of course, but strip the dura from it. Then on one patient I sectioned the sensory root by the posterior approach. I was nowhere near the ganglion, I could not have disturbed it, and that individual had the most extensive herpetic lesions on the lower half of the face of any patient I have ever seen. So it is not due to direct trauma to the gasserian ganglion.

DR. A. EARL WALKER, Chicago: In view of the fact that the denervated areas are commonly said to be particularly susceptible to infection and injury, it is remarkable that following retrogasserian neurectomy so few cases such as have been described today are reported. From France in 1936 Dechaume and Delibéros (*Rev. de stomatol.* **38**:194 [March] 1936) reported an ulcerative lesion of the maxillary mucous membrane of a patient who, twelve years before, had a retrogasserian neurectomy. They stated that such a complication was unique in their experience. In their case trauma was probably a precipitating factor, as Dr. Peet has emphasized, for the patient had worn an ill fitting denture which bothered her a great deal. I am more interested in the type of sensory disturbance which the authors have discussed. It has been shown that section of the descending root of the trigeminal nerve, in the manner Sjöqvist devised, produces sensory changes, a marked analgesia with relative hypesthesia in the divisional portions of the face; that is, it involves the first, second or third division but does not give rise to the onion skin type of sensory disturbance which is seen occasionally in syringobulbia. Neuro-anatomy does not tell the reason for this difference, although it has now been shown that there is a definite laminar arrangement of the tracts derived from both the nucleus of the descending portion of the trigeminal nerve and the main trigeminal nucleus. The onion skin type of sensory disturbance is analogous to the stocking or glove type of sensory disturbances in the arms or legs. We know that such sensory disturbances do not usually occur with spinal cord lesions, but they are seen with lesions of the thalamus and cerebral cortex. This suggests that there is a rearrangement of the nerve fibers in their passage from the spinal cord to the thalamus and to the cortex. It is quite probable that such a rearrangement of the fibers occurs very shortly after their origin in the spinal cord or from the descending root in the fifth nerve. Hence, as Sjöqvist, Smyth, Stratford and others have suggested, syringobulbia involving the secondary trigeminal pathways would give rise to the type of sensory disturbance which is more commonly seen with lesions of the thalamus or cerebral cortex than the type of impairment which is seen with section of the primary sensory nerve fiber.

DR. BYRON STOOKEY, New York: I should like to confirm what Dr. Peet said. In a large series of trigeminal operations I have not encountered the type of lesions presented to us this morning. The only trophic disturbances, if they are trophic disturbances, that I have seen have been the ones Dr. Peet has described following the operation immediately, and then there has been another group of which I should think there are about seven or eight cases of so-called seborrheic dermatitis, a scaly, greasy condition found over the distribution of the fifth nerve, mostly in the first division, to a less extent in the second division, in those instances in which we have done a total section. With these two exceptions I have not encountered the type of lesion which has been presented. I am extremely interested in the presentation. I question whether we can call it trophic disturbances and I wondered, in view of the extreme rarity of the lesions following dorsal section, if they are necessarily alone to be attributed to the cutting of the fifth nerve root.

MELANOMA OF THE CENTRAL NERVOUS SYSTEM

REPORT OF THIRTY-FOUR CASES, IN NINETEEN OF WHICH THE DIAGNOSIS WAS VERIFIED BY OPERATION OR NECROPSY

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During the five weeks from April 1 to May 5, 1939, inclusive, we had occasion to make a diagnosis of melanoma of the central nervous system in four cases. The rapid succession of these four tragic experiences prompted us to carry out the present study.

A survey of the literature on melanoma reveals an almost endless list of contributions covering various phases of the subject. In this presentation we are not concerned with the histologic structure of melanoma but wish to stress the importance of melanoma from the neurologic standpoint. We are employing the terms "melanoma," "melanocarcinoma," "melanosarcoma" and "melano-epithelioma" synonymously.

That melanomas are a serious menace to life needs no comment. The frequency of their occurrence remains somewhat uncertain. Adair[1] reported that 400 cases were observed at the Memorial Hospital in Chicago during an eighteen year period. In 41,984 surgical specimens examined by the department of pathology at the Toronto General Hospital from January 1928 to January 1935 Plewes[2] found ninety-three melanomas, or an incidence of 0.2 per cent. Affleck,[3] in a follow-up study of 170 patients who had melanomas, found that 115 died in less than three years and that 10 per cent were alive after a lapse of five years. Broders and MacCarty[4] in their review said that the mortality rate was 86.8 per cent although they said that all their patients had not been heard from.

Two contributions on melanomas of the nervous system, one by the Wortises[5] in 1936 and the other by Courville and Schillinger[6] in 1939, leave little to be added to the general consideration of the subject. It may be well, however, again to call attention to the frequency with which melanomas involve the central nervous system and to urge rigid prophylaxis against this disease. As Adair has stated, "there is no tumor which places the clinician in such a mental state of helplessness as the melanoma once it has left the original site." The frequency with which melanomas metastasize to the central nervous system varies from 10 to 50 per cent according to different authors. In a series of 20,000 necropsies Courville and Schillinger noted twenty instances of melanoma; in eighteen of the cases there

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Read before the Section on Nervous and Mental Diseases at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Adair, F. E.: Treatment of Melanoma: Report of Four Hundred Cases, Surg., Gynec. & Obst. **62**: 406-409 (Feb. 15) 1936.
2. Plewes, F. B.: Malignant Melanomatosis, Am. J. Cancer **26**: 732-737 (April) 1936.
3. Affleck, D. H.: Melanomas, Am. J. Cancer **27**: 120-138 (May) 1936.
4. Broders, A. C., and MacCarty, W. C.: Melanoma-Epithelioma: A Report of Seventy Cases, Surg., Gynec. & Obst. **23**: 28-32 (July) 1916.
5. Wortis, Herman, and Wortis, S. B.: Metastatic Melanoma Involving the Central Nervous System, Arch. Neurol. & Psychiat. **36**: 601-611 (Sept.) 1936.
6. Courville, C. B., and Schillinger, R. J.: Metastatic Melanoblastomas of the Brain: Review of the Literature and Survey of Eighteen Cases, Bull. Los Angeles Neurol. Soc. **4**: 8-22 (March) 1939.

was widespread metastasis. In nine, or 50 per cent, of the eighteen cases, the brain was involved. Bailey [7] suggested a similar figure for involvement of the brain in the presence of generalized metastasis. He stated, however, that this figure may be somewhat high. In 1932 Dunlap,[8] in a report of ninety-five metastatic tumors of the brain observed at the Mayo Clinic, said that he found only two melanomas. As a result of our present study this figure should be increased by several cases. In a series of 107 cases of metastatic tumor of the brain, Courville and Schillinger observed that the incidence of melanomas was 13 per cent.

MATERIAL

In the ten year period from 1930 to 1939 inclusive we have seen approximately 500 cases of melanoma. This number represents about 2 per cent of the total number of cases of malignant lesions seen during that period. Unfortunately a complete follow-up study in the 500 cases has not been possible; therefore accurate deductions cannot be made. In approximately a fourth of the cases of melanoma the primary tumor was situated in or about the eye. In at least 347 of the 500 cases there was evidence of local recurrence or metastasis at the time the patients were last seen at the clinic. The majority of these patients have died. In at least thirty-four, or 10 per cent, of the 347 cases there was clinical evidence of melanotic involvement of the central nervous system.

CLINICAL AND PATHOLOGIC CONSIDERATION

In twenty-four cases the brain was the site of the melanomic involvement. In ten cases the spinal cord was affected. In one instance both the brain and the spinal cord were affected. In nineteen of the thirty-four cases the diagnosis was verified by microscopic examination of a specimen removed from the brain or spinal cord at operation or by necropsy (table 1). In the remaining fifteen cases necropsy was not performed or did not include examination of the central nervous system. However, biopsy disclosed that the primary tumor was a melanoma; clinical signs and symptoms were indicative of involvement of the central nervous system and there usually was evidence of generalized metastasis. We have excluded from this study twenty-four additional cases which with but a slight stretch of the imagination might well be included in this category but, because of the absence of postmortem or operative confirmation, must be excluded. It does seem proper to call attention to this additional group because in a study of this type one cannot fail to be impressed by the fact that metastatic involvement of the central nervous system by melanomas is much more common than is generally appreciated. If these twenty-four cases had been included it would have been found that the central nervous system was involved in 20 per cent of the cases of melanoma in which generalized metastasis had occurred. This incidence is less than half of that reported by Courville and Schillingere and by Bailey. This difference may be attributable to our inability to obtain accurate follow-up data.

There are several good reasons for the failure to appreciate the importance of melanotic involvement of the central nervous system. Following a diagnosis of melanoma with evidence of metastases, the patient is frequently taken home and dies without a postmortem examination. Again, in the absence of a primary melanoma of the skin or in some other obvious site a patient may die without a proper diagnosis and the correct diagnosis may be established only by necropsy, which is performed only occasionally (Plewes). The very late occurrence of metastasis from a primary melanoma may also lead to an incorrect diagnosis. In our series of cases the correct diagnosis would have been overlooked in at least twelve instances had the patient failed to come to operation or necropsy. From these statements it must be appreciated that the statistics on the involvement of the central nervous system by melanoma are rather inaccurate. Twelve of the thirty-four patients died while under observation at the clinic; in ten of the twelve cases necropsy was performed. Seventeen patients died at home; necropsy was performed in four of these cases. The remaining five patients could not be followed.

Of the thirty-four patients, twenty-three were males and eleven were females. Twenty-nine patients are known to be dead and in five cases follow-up data were not available. Necropsy was performed in fourteen of the twenty-nine cases in which death is known to have occurred. In seven of the fourteen cases necropsy was not complete, and in another case, in which necropsy was performed at the patient's home, no mention was made of postmortem examination of the brain or spinal cord. In three of the seven cases neither the brain nor the spinal cord was examined at necropsy and in four cases examination of one of these structures was omitted. Operation was performed in eleven cases, in six for tumor of the brain and in five for tumor of the spinal cord. It is noteworthy that in twelve cases the presence of a melanoma was not suspected prior to operation or necropsy. In eight of the twelve cases no primary melanoma was discovered. In three cases, after the melanoma in the nervous system was found the patient or the family revealed that a mole had been removed previously. In the remaining case the eye had been enucleated some time previously. A diagnosis of glaucoma had been made but because of the subsequent course of events the eye undoubtedly must be considered as the site of a primary melanoma. This group of twelve cases indicates the need of constantly bearing in mind the possibility of a melanoma in the presence of a rapidly progressive disorder of the central nervous system. Great care must also be exercised in the examination of patients suspected of having melanoma and whenever possible any available material should be submitted for microscopic examination.

The ages of the patients at the time of examination at the clinic because of symptoms referable to the central nervous system ranged from 4 years to 66 years. Twenty-two of the thirty-four patients were in the fourth to the sixth decade of life inclusive. The length of time from the excision of the primary melanoma or mole to the death of the patient varied from four months to thirteen years. The average duration was approximately two and a half years. As far as we could determine, the majority of the primary moles had been removed surgically but the mole had been removed some time after evidence of rapid growth had developed. It is pertinent to this problem to insist that moles situated in places subject to irritation should be excised before they show any signs of "wildness." The site of the known primary mole was as follows: back, ten cases; head, face and neck, five cases; eyes, six cases; heel, two cases; hand, one case; umbilicus, one case; labium, one case, and unknown, eight cases. From our studies no definite statement can be made concerning

7. Bailey, Percival: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1933.
8. Dunlap, H. F.: Metastatic Malignant Tumors of the Brain, Ann. Int. Med. 5: 1274-1288 (April) 1932.

TABLE 1.—*Clinical and Postmortem Data in Thirty-Four Cases of Melanoma of the Central Nervous System*

Case and Sex	Age, Years: When Mole Was Excised	Age, Years: At Death	Site of Primary Mole	Duration of Neurologic Symptoms Before Visit to Clinic	Clinical Diagnosis	Neurologic Symptoms	Clinical Course	Postmortem Observations	Comment
1 ♂	39	40	Neck	2½ weeks	Metastatic melanoma of brain	Headache, diplopia and progressive delirium for 2½ weeks; no papilledema	Died 5 days after registration	Multiple melanomas of brain; largest tumor in left temporal lobe; generalized metastasis to organs of body	
2 ♂	..	61	Back	2 months	Melanoma not suspected	Mental confusion and progressive weakness for 2 months; terminal coma; papilledema	Died 3 days after registration	Brain not examined; melanoma in spinal meninges; generalized metastasis to organs of body	Mole not discovered until after death
3 ♀	33	36 (?)	Back	4 months	Metastatic melanoma of brain	Headache, weakness and confusion for 4 months; papilledema of 3-4 diopters	Returned home after operation; condition became progressively worse; no final information	.....	Operation disclosed melanoma of left frontal lobe
4 ♂	62	63	Heel	6 weeks	Metastatic melanoma of brain	Dizziness, vomiting and ataxia for 6 weeks; terminal stupor; no papilledema	Died 2 weeks after registration	Multiple melanomas of cerebrum and cerebellum; spinal cord was not examined; generalized metastasis to organs of body	
5 ♂	41	43	Eyelid	6 months	Melanoma not suspected	Deafness, headache, vomiting and ataxia for 6 weeks; no papilledema	Returned home and died 1 year later	.....	Operation disclosed melanoma of left frontal lobe; mole on eyelid was not recorded in history
6 ♂	..	55	?	1 day	Melanoma not suspected	Left hemiplegia developed gradually 10 days after an exploratory laparotomy	Patient died of cerebral thrombosis (?) 10 days after operation	Multiple melanomas in cortex and ventricles; generalized metastasis to organs of body; site of primary tumor unknown	Exploratory laparotomy disclosed a melanoma
7 ♀	37	?	?	8 months	Melanoma not suspected	Fatigue, headache, failing vision, incoordination and mental dulness for 8 months; papilledema of 5 diopters	Died one day after craniotomy	One large melanoma of left frontal lobe; primary in brain (?); no melanomas in other organs	
8 ♂	..	49	?	7 months	Melanoma not suspected	Signs and symptoms of compression of spinal cord at first thoracic segment for 7 months	Returned home and died 2 months later	.....	Laminectomy and biopsy disclosed a melanoma
9 ♂	38	41	Back	2 months	Melanoma not suspected	Numbness of right arm for 2 months; this was followed by jacksonian convulsions; coma for 4 days before death	Patient died of bronchopneumonia 24 hours after admission	Melanoma (5 cm.) in left parietal lobe; ependymoma of fourth ventricle; melanomas in other organs	History of primary mole not obtained until after necropsy
10 ♂	..	34	?	8 years (?)	Melanoma not suspected	Hemangioma of the cervical segment of the spinal cord suspected and exploratory operation performed 9 months before patient came to clinic; symptoms had progressed; no spinal subarachnoid block; examination of spinal fluid disclosed 50 mg. of protein per 100 cc. and 56 lymphocytes per cubic millimeter	Patient died at home	.....	Another exploratory operation on cervical segment of spinal cord disclosed a melanoma; 4 months later an exploratory laparotomy at home revealed multiple melanomas
11 ♂	..	31	?	2½ months	Melanoma not suspected	Increasing headache, blurred vision and syncopal attacks for 2½ months; papilledema of 4 to 6 diopters; no localizing signs	Died 1 day following exploratory craniotomy	Large melanoma of third ventricle, which extended to the fourth ventricle, pons and medulla; only the head examined	
12 ♂	66	67	Eye	3 months(?)	Metastatic melanoma of brain	Headache and weakness following enucleation of eye for melanoma; local recurrence of the tumor; no neurologic examination	Died 2 days after admission	Melanoma of right occipital lobe; extension to arachnoid and dura; generalized metastasis to organs of body	
13 ♂	17	19	Neck	4 months	Metastatic melanoma of brain	Headache, spells of unconsciousness and diplopia for 4 months; papilledema of 5 to 6 diopters	Condition became worse after patient went home; patient died 6 months later	.....	Melanoma removed from left frontal lobe
14 ♂	..	63	?	4 years	Melanoma not suspected	History of progressive lesion of spinal cord for 4 years; partial spinal subarachnoid block; 100 mg. of protein per 100 cc. of spinal fluid	Was alive 2 years after operation; final follow-up data not obtained	.....	Laminectomy and biopsy disclosed a melanoma
15 ♀	..	55	?	3 years	Melanoma not suspected	History of progressive compression of spinal cord at level of fifth thoracic segment; complete spinal subarachnoid block; 1,300 mg. of protein per 100 cc. of spinal fluid	Condition of patient was critical 4 months after she returned home	.....	Laminectomy and biopsy disclosed a melanoma
16 ♀	..	16	?	6 weeks	Melanoma not suspected	Headache, vomiting and papilledema of 4 to 5 diopters for 6 weeks	Died 1 year later at home	.....	Exploratory operation and biopsy disclosed melanoma of cerebellum
17 ♀	40	44	Umbilicus	5 months	Metastatic melanoma of brain	Headache, mental cloudiness and spells of unconsciousness for 5 months; no papilledema	Returned home and died 10 days later	Single melanoma, 3 cm. in diameter, in left parietal lobe; spinal cord not examined; no pathologic report of melanomas in other parts of body	Biopsy at home had revealed that mole was benign; biopsy of lymph node disclosed melanoma

TABLE 1.—*Clinical and Postmortem Data in Thirty-Four Cases of Melanoma of the Central Nervous System—Continued*

Case and Sex	Age, Years: When Mole Was Excised	Age, Years: At Death	Site of Primary Mole	Duration of Neurologic Symptoms Before Visit to Clinic	Clinical Diagnosis	Neurologic Symptoms	Clinical Course	Postmortem Observations	Comment
18 ♂	55	56	Eye	3 months	Metastatic tumor of spinal cord and brain (?)	Eye had been enucleated 9 months previously for glaucoma (?); no pathologic examination; severe facial pain with anesthesia for previous 3 months; signs of compression of spinal cord for 6 weeks; partial spinal subarachnoid block; spinal fluid yellow; 1,800 mg. of protein per 100 cc. of spinal fluid	Returned home and died 3 months later	Generalized melanomas in organs of body; brain and spinal cord not examined	Laminectomy and biopsy disclosed a melanoma
19 ♂	32	33	Eye	6 weeks	Melanoma not suspected	Eye had been enucleated 1 year previously; no pathologic examination; general weakness, absence of knee jerks and attacks of coma for 6 weeks	Condition gradually became worse; patient died 3 weeks after registration	Multiple small melanomas of meninges and bones of skull; generalized metastasis to organs of body	
20 ♂	37	44	Conjunctiva	6 weeks	Metastatic melanoma of brain (?)	Headache, vertigo, incoordination and mental cloudiness for 6 weeks; papilledema; roentgenogram of thorax disclosed metastatic lesions	Returned home and died 2 weeks later	.....	Course of roentgen therapy to head
21 ♀	54	59	Heel	5 months	Metastatic melanoma of brain (?)	Progressive mental change, weakness of left side and left homonymous hemianopia for 6 months	Returned home and died 1 month later	.....	No treatment at clinic
22 ♂	49	55	Scalp	6 weeks	Metastatic melanoma of brain (?)	Progressive weakness of left arm for 6 weeks; blurred vision and vomiting occurred later	Follow-up data not available	.....	No treatment at clinic; 3 small melanomas on left choroid
23 ♂	42	45	Back	3 months	Metastatic melanoma of spinal cord (?)	Lumbar root pain for 3 months; transverse myelitis	Returned home and died 3 months later	.....	Symptomatic treatment
24 ♂	61	63	Nose	3 weeks	Melanoma of spinal cord (?)	Increasing back pain and progressive weakness for 3 weeks	Returned home and died 3 months later	Generalized melanoma of organs of body; vertebral column and spinal nerves involved; brain and spinal cord not examined	Symptomatic treatment at clinic
25 ♀	14	24	Back	3 months	Metastatic melanoma of brain (?)	History of headache; increasing confusion, choked disks and coma for 3 months	Died 2 days after registration		
26 ♂	42	43	Back	6 weeks	Melanoma of spinal cord (?)	Increasing numbness and weakness of legs for 6 weeks	Returned home and died 6 weeks later; transverse myelitis	.....	No treatment at clinic
27 ♀	4	4	Eye	2 months	Metastatic tumor of brain (?)	Enlargement of globe of left eye for several months; enucleation of eye; headache and pain in legs developed later	Mass developed on occiput; patient failed gradually and died at home 2 months after registration	.....	Radium applied to left orbit
28 ♂	52	53	Back	4 weeks	Metastatic melanoma of brain (?)	Headache, progressive aphasia and weakness for 4 weeks; roentgenogram of thorax suggested metastatic involvement	Patient returned home; no follow-up data	.....	No treatment at clinic
29 ♀	45	46	Labia	4 weeks	Metastatic melanoma of brain (?)	Progressive aphasia and generalized weakness for 4 weeks; coma	Died following symptomatic treatment for 2 weeks		
30 ♀	50	54	Back	6 months	Metastatic melanoma of spinal cord (?)	Progressive weakness of left arm for 6 months; roentgenograms disclosed metastatic involvement of thorax and spinal column	Returned home and died 3 months later	.....	No treatment at clinic
31 ♂	60	63	Thumb	6 months	Metastatic melanoma of spinal cord (?)	Progressive back pain with extension to sciatic region for 6 months; roentgenogram showed metastatic involvement of sacrum	Returned home and died 6 months later	.....	No treatment at clinic
32 ♂	40	41	Face	5 weeks	Metastatic melanoma of brain (?)	Progressive weakness of left arm for 5 weeks; several jacksonian convulsions; metastatic involvement of thorax	Progressive coma and death	Generalized metastasis to organs of body; brain and spinal cord not examined	
33 ♀	25	27	Back	7 weeks	Metastatic melanoma of brain (?)	Increasing headache, diplopia and vomiting for 7 weeks; rigidity of neck; choked disks of 4 to 5 diopters; metastatic involvement of thorax	Patient returned home and died 4 weeks (?) later	.....	No treatment at clinic
34 ♂	35	35	Back	.....	Metastatic melanoma of brain (?)	Mole removed from back 1 year before registration; generalized melanin pigmentation for 2½ months; melanin in urine	Returned home; had several convulsions; died 4 months later	Necropsy at home; generalized metastasis but no statement about central nervous system	Lead treatment

the presence of other moles. The length of the time the mole was present before removal varied from one to thirty-eight years. A few patients stated that the mole had always been present. As a rule some fourteen months had elapsed between the removal of the initial mole and the first signs of metastasis. Unfortunately we have no definite information regarding the many moles which may have been removed without development of metastases at some later date. As can be seen from table 1, a fair percentage of our patients apparently had an involvement of the central nervous system by melanoma prior to involvement of the other organs of the body. If organs other than the central nervous system were involved first, subsequent involvement of the central nervous system, if it did develop, usually occurred in about two months. In four of the thirty-four cases the primary melanoma occurred in the choroid of the eye. It is interesting to note that during the ten year period under consideration there have been observed at the clinic 125 cases of melanoma of the eye in which enucleation was performed either here or elsewhere. Strangely enough, our figures are not in keeping with those of some of the other writers who maintain that melanoma of the eye is especially prone to metastasize to the central nervous system. Had we been able to obtain follow-up data in the entire group of 125 cases of melanoma of the eye we probably would have discovered more than four instances of involvement of the central nervous system, but apparently the percentage is relatively small. Our observations are in keeping with those of Benedict,[9] who said that melanoma of the choroid tends to metastasize to other organs of the body, especially the liver, in preference to the central nervous system. Terry and Johns,[10] in a review of ninety-eight cases of melanoma of the eye, noted that the diagnosis was incorrect in forty-two instances. The diagnosis in these forty-two cases was glaucoma, opaque cornea, inflammatory lesion and so on and the correct diagnosis was made only by biopsy.

TABLE 2.—*Results of Examination of Cerebrospinal Fluid in Five Cases of Melanoma of the Spinal Cord*

	Case 8	Case 10	Case 14	Case 15	Case 18
Total protein, mg. per 100 cc.	50	100	120	1,200	1,000
Color or transparency.....	Clear	Clear	Yellow	Yellow	Yellow
Spinal-subarachnoid block...	...	Partial	Partial	Complete	Partial

In only one of the thirty-four cases in our series was there metastatic involvement of both the brain and the spinal cord. In three cases the melanoma appeared to be primary in the brain and in three cases it appeared to be primary in the spinal cord. In these six cases operation was performed and the diagnosis of melanoma was made by biopsy. Four of the six patients are known to have died. A complete necropsy was possible in one case and partial necropsy was performed in another case. Two of the six patients were alive at the time the last follow-up data were obtained. In none of these six cases did any signs of metastasis develop. In the case in which complete necropsy was possible the primary melanoma undoubtedly involved the central nervous system. In the other five cases (one of which was reported previously by one of us[11]) the available data certainly suggested that the primary melanoma involved the central nervous system.

In eleven of the twenty-four cases of melanoma of the brain the outstanding clinical symptoms, such as mental dulness, confusion, coma and delirium, pointed to involvement of the brain. As emphasized by Craig and one of us[12] the neurologic diagnosis may present various difficulties because of the mental status of the patient and the diffuse character of the symptoms. In two cases the clinical picture was confused by the presence of a bromide psychosis or drug intoxication. Several of the patients were moribund when they were brought to the hospital and the correct diagnosis was made only at necropsy. The cerebrospinal fluid was examined in three cases of melanoma of the brain. In two cases the fluid was entirely normal. In the remaining case the value for the total protein was 50 mg. per hundred cubic centimeters of fluid and there were sixty-seven lymphocytes in each cubic centimeter of fluid. The results of examination of the cerebrospinal fluid in five cases of melanoma of the spinal cord are shown in table 2. In no instance was melanin discovered in the spinal fluid.

Roentgenographic examination of the skull was of little value in the diagnosis of melanoma of the brain. In five instances roentgenographic examination of the thorax showed evidence of metastatic involvement and in two additional cases the results of such examination were suggestive of metastatic involvement. Contrary to the usual statement concerning involvement of the bone, we have seen melanotic erosion of the vertebrae, the sacrum and the skull in three cases. Nine of the thirty-four patients showed clinical signs of generalized metastasis when examined at the clinic. Loss of weight was a common symptom. In five cases the sedimentation rates of the erythrocytes were 10, 18, 24, 64 and 109 mm. at the end of one hour, respectively. In only one instance was melanin discovered in the urine, but tests for melanin in the urine were not carried out as a routine in this series of cases.

At times a melanoma may be associated with an acoustic neuroma.[13] Björneboe[14] has observed the association of melanoma with von Recklinghausen's disease. Occasionally, diffuse melanosis of the skin as reported by Odel and his co-workers[15] (fig. 1) will give the clue to the correct diagnosis. Space will not permit of a lengthy consideration of the individual cases, each one of which presented some interesting diagnostic and clinical problem. The clinical and pathologic data in these cases are shown in table 1.

COMMENT

In considering melanomas it must be emphasized that the frequency of their occurrence in the central nervous system is much greater than is generally recognized. While metastasis usually occurs within a few years after removal of the primary melanoma, as many as ten or even twenty-five years may elapse between removal of a primary melanoma and metastatic involvement of the central nervous system or of other organs of the body. This late development of metastatic melanoma must be kept in mind in any statistical study, for undoubtedly many patients who have melanoma die years after the

9. Benedict, W. L.: Personal communication to the authors.
10. Terry, T. L., and Johns, J. P.: Uveal Sarcoma—Malignant Melanoma: Statistical Study of Ninety-Four Cases, Am. J. Ophth. **18**: 903-913 (Oct.) 1035.
11. Da Costa, D. G., and Love, J. G.: Primary Melano-Epithelioma of the Spinal Cord, Proc. Staff Meet., Mayo Clin. **14**: 628-631 (Oct. 4) 1939.
12. Craig, W. McK., and Kernohan, J. W.: Melano-Epithelioma of the Brain (Metastatic), S. Clin. North America **12**: 989-999 (Aug.) 1932.
13. Bair, H. L., and Love, J. G.: Acoustic Neurofibroma Associated with Melano-Epithelioma of the Choroid: Successful Removal of Both Tumors, Proc. Staff Meet., Mayo Clin. **12**: 481-485 (Aug. 4) 1937.
14. Björneboe, M.: Primäres Melanosarkom des Gehirns, massenhafte Naevi pigmentosi der Haut, ausgedehnte Neurofibromatose der Hautnerven, Frankfurt. Ztschr. f. Path. **47**: 363-373, 1934.
15. Odel, H. M.; Montgomery, Hamilton, and Horton, B. T.: Diffuse Melanosis Secondary to Malignant Melanoma: Report of Case, Proc. Staff Meet., Mayo Clin. **12**: 742-747 (Nov. 24) 1937.

removal of the primary mole or melanoma with an incorrect diagnosis. It is of considerable interest, as noted by Knight,[16] Adair and others, that a patient with a melanoma of the eye may survive enucleation of the eye for many years and when metastasis does occur it tends to occur elsewhere than in the central nervous system, especially in the liver. The incidence of metastasis to the central nervous system from melanomas of the eye has been unusually rare in our series of cases as compared to that reported in the literature. One reason for the apparent good prognosis in cases of melanoma of the eye is that the lesion is recognized rather early as a result of the disturbance of vision and the melanoma is removed before extension or metastasis occurs.

It is evident from a survey of our postmortem material that metastatic melanoma may occur throughout the organs of the body without involvement of the central

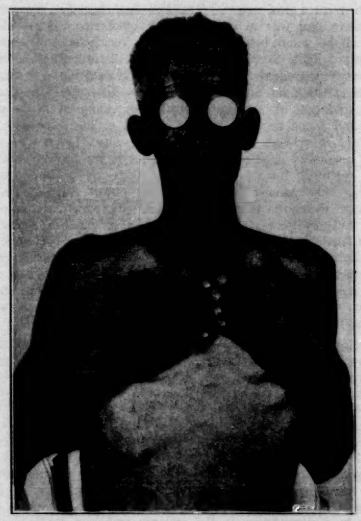

Fig. 1.—Diffuse melanosis of skin.

nervous system, and, similarly though to a lesser degree, the brain or spinal cord may be the only site of metastatic involvement.

As noted by Courville and Schillinger, Plewes and others, involvement of bony structures by melanoma has been comparatively rare. When it has occurred it invariably has resulted from direct extension of the melanotic growth. In an appreciable number of cases we have witnessed involvement of the brachial plexus and lumbosacral plexus by melanotic extension or by metastasis.

In the differential diagnosis of melanoma it must be remembered that the patient or relatives frequently will fail to mention the previous removal of a mole. As a rule, such information is withheld unintentionally but in a few cases in our series the knowledge of a mole was deliberately withheld because of the previous unfavorable prognosis. As has been emphasized by Bailey, when a middle-aged person has a rapidly progressing mental or nervous disease and the usual conditions such as vascular disease, inflammatory affliction may be ruled out, it is important to consider seriously the possibility of melanoma of the central nervous system.

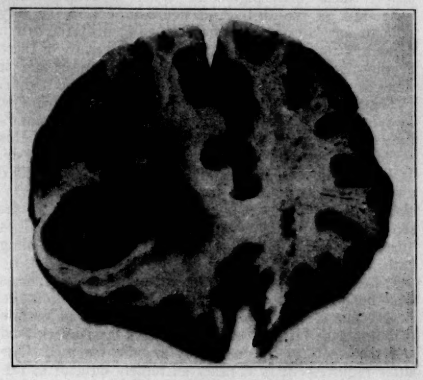

Fig. 2.—Melanoma of brain.

Although at present there seems little that can be accomplished by operation in cases of melanoma of the central nervous system, one should not adopt a defeatist attitude with regard to this serious affliction. In a small percentage of cases a great deal of palliative relief, even if not actual cure, can be obtained by radical operation. If the melanoma is primary in a so-called silent area of the brain, radical surgical removal may be justified; if the lesion is single and nodular, even though metastatic, complete removal may be possible. If the lesion cannot be extirpated from the brain (fig. 2) a palliative subtemporal decompression may afford relief from the increased intracranial pressure and its consequent headache, vomiting and failing vision.

If the melanoma is intraspinal and does not invade the spinal medulla (fig. 3), complete removal is pos-

Fig. 3.—Melanoma of spinal cord.

sible. Even if it involves one or more nerve roots, these might be sacrificed in a radical surgical procedure without endangering the patient's life. If the spinal cord or intraspinal nerve roots are involved by a neoplasm, and if the tumor is not too extensive, a subtotal removal is not only justifiable but definitely indicated to ameliorate the patient's symptoms.

16. Knight, Mary S.: Melanotic Neoplasms of the Eye, J. A. M. A. 83: 1062-1068 (Oct. 4) 1924.

We do not wish to enter into a discussion of the microscopic appearance of melanomas, but there are several points worth considering. It is generally considered by pathologists that nonpigmented or sparsely pigmented melanomas are more malignant than those deeply laden with pigment. When a nonpigmented melanoma is found by the neurosurgeon it is very difficult for him or the pathologist to identify the origin of such a tumor. The melanin content of many of these neoplasms varies from one region to the next and at times it varies in degree in the same metastatic nodule.

These tumors may spread either by blood stream or by lymphatics and usually by both; the original tumors have a tendency to invade blood spaces early and this explains their wide dissemination throughout the body. It is difficult to understand why in some cases there may be a latent period of many years between the excision of the original tumor and the appearance of the secondary masses. This late recurrence of metastasis is misleading and disconcerting to all concerned in dealing with the problem.

It has been shown in a sufficient number of instances that melanomas arise primarily from the meninges. Before one can accept such a case one must be certain that no small primary skin tumor has been overlooked and that there is no metastasis to other organs. The latter requirement is at times extremely difficult to fulfil on clinical and roentgenologic grounds alone, and without a thorough search at necropsy such a case should be accepted with reservation. In six cases in our series we were of the opinion that the tumors occurred primarily in the central nervous system but because of lack of necropsy we can only say that they possibly originated in the meninges. We were able to prove to our own satisfaction that one tumor was primary in the central nervous system.

CONCLUSIONS

1. Melanoma of the central nervous system is a diagnosis that must be reckoned with by the neurologist.

2. Careful inquiry about the removal of pigmented lesions should be carried out and, if possible, any available material should be reexamined for the presence of melanoma.

3. It must be realized that a melanoma occasionally may be primary in the central nervous system and that in the presence of any rapidly progressive lesion of the central nervous system such a diagnosis must be seriously considered.

4. While it is not in the realm of the neurologist to advise patients regarding lesions of the skin, the opportunity of preaching prophylaxis in the presence of pigmented moles must not be overlooked.

ABSTRACT OF DISCUSSION

DR. S. BERNARD WORTIS, New York: Dr. Moersch and his associates have emphasized the serious nature of melanoma of the central nervous system. Some years ago we reported several from the Bellevue Hospital and can only confirm the observations of Dr. Moersch and his group. Our patients were all over 50 years of age. Papilledema was common. In some of our patients the cerebrospinal fluid was bloody and in a few we were able to find melanin pigment or melanin cells in the spinal fluid. One point worthy of emphasis is that the time between the onset of original irritation of the melanotic focus and the onset of cerebral symptoms varies from eight to ten years, whereas the time elapsing from the onset of cerebral symptoms to death is much shorter, in our series from seven days to two or three months. Many of the symptoms are those referable to disseminated lesions in the nervous system simulating diffuse meningo-encephalopathy. Since a third of all melanomas originate in the choroid of the eye, a syndrome can be established wherein one can distinguish four clinicopathologic stages in the course of such tumors. The first stage consists of detachment of the retina by the melanotic tumor and is associated with impairment of vision, a defect in the visual field or complete blindness of one eye. The second stage consists of the period of increasing intra-ocular tension associated with pain. This condition of the eye often resembles glaucoma. However, it can be differentiated from glaucoma by the fact that melanosarcoma is preceded by blindness and the patient subsequently has pain. In glaucoma pain comes first and blindness is a subsequent occurrence. Subsequent stages give evidence of diffuse involvement of other organs. When the liver is involved in these people the urine gives a positive test for melanuria. I agree with Dr. Moersch and his group that these people require early treatment of the primary focus, and this caution cannot be overemphasized.

DR. PETER BASSOE, Chicago: A man whom I saw when he was 40 years old was known to have had syphilis, had been treated for many years and had become Wassermann negative and was in perfect health until two weeks before I saw him, when he was taken with headache and vomiting, followed by a convulsion and aphasic disturbance. A lumbar puncture was made. The Wassermann reaction was negative with spinal fluid and blood. A few days after the onset I was told that his eyegrounds had been examined in the morning and found normal. In the evening of the same day there were hemorrhages in both eyes, and when I saw him there was a marked papilledema with hemorrhages. We disregarded the syphilitic history and made a diagnosis of tumor of the brain. The patient lived only a few days. Autopsy revealed a large melanotic tumor on the left side, which accounted for the focal symptoms and two other similar tumors which confirm Dr. Moersch's statement that nothing can be done surgically with these tumors. Aside from the vomiting, which undoubtedly was due to the brain lesion, this man had never had anything to call attention to his abdomen. The autopsy, which was complete, showed that the primary tumor was a melanotic carcinoma of the pancreas.

DR. HANS H. REESE, Madison, Wis.: I believe that melanoma belongs to the large group of von Bogaert's congenital neuroectodermal dysplasias: (1) tuberose sclerosis, (2) neurofibromatosis of von Recklinghausen, (3) angiomatosis and (4) ectodermal dystrophies (xerodermal idiocy, heredofamilial keratoses, congenital generalized ichthyosis. I wish to ask the authors whether or not they considered the melanoma as a subdivision of the status pigmentatus. Von Bogaert of Antwerp is correct in assuming that the various groups are one and the same group but with different tissue selectivity. If the tissue selectivity occurs in the form of a skin melanoma there may be a disturbance in the melanin and iron containing pigment distribution; therefore a radical surgical intervention would remove only a localized metabolic dysplasia of the melanic pigment. I can't see any reason to interfere surgically with a skin lesion. I do not know whether the authors meant that all primary melanomas should be operated on early. Clinical observation reveals that melanomas grow or metastasize with rapidity on intervention. One cannot make the diagnosis of generalized tissue melanoma. Do you consider a melanoma as being a melanosarcoma or do you regard a localized melanoma only as a specific pigment accumulation in the ectoderm? The various infiltrations of leukemia or of xanthoma do not cure the basic disturbances even if localized lesions are removed. Do you know whether any spectrolytic observations are known which support an early diagnosis of suspected melanoma and which would eliminate a biopsy? Did you find in your postmortem examinations any increased pigmentations in the globus pallidus, rubra zone, substantia nigra and locus coeruleus? I should like Dr. Moersch to answer the question How do you treat a localized melanoma especially in view of the high probability of metastases?

DR. FREDERICK P. MOERSCH, Rochester, Minn.: The remarks of Dr. Wortis regarding melanoma of the eye are well taken. It is interesting how frequently melanomas of the eye will

metastasize to the liver and not to the brain. As Dr. Bassoe pointed out, many of these patients come in with a very short history. As a matter of fact, some of our patients were brought into the hospital in a state of coma, and not until postmortem examination was the melanoma discovered. In the paper I purposely avoided the possibilities that Dr. Reese suggested because I believe it becomes an exceedingly controversial subject as to what one man considers a melanoma and what is considered melanoma by another. I am sorry Dr. Kernohan is not here to answer the questions of Dr. Reese. I am sorry I cannot.

A PREPARATION OF TOXIN SUITABLE FOR ORAL IMMUNIZATION AGAINST SCARLET FEVER

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AND
GLADYS HENRY DICK, M.D.
CHICAGO

That sterile scarlet fever toxin administered by mouth may result in satisfactory immunization was reported in 1932.[1] This observation was first made during attempts to learn whether or not some of the so-called intestinal rashes mentioned as occurring in children might be caused by milk which had been contaminated with a scarlet fever streptococcus and subsequently pasteurized at a temperature which kills the streptococci but does not destroy the toxin.

In these first experiments it was found that transient scarlatinal rashes might occur in susceptible persons when comparatively large doses of the sterile toxin were ingested. Subsequent cutaneous tests showed modification of the susceptibility, indicating the production of some degree of antitoxic immunity.

This observation led to further experiments in which sterile toxin, containing 0.5 per cent phenol, was administered by mouth in graduated doses. The results indicated that, if enough toxin was given, a degree of immunity sufficient to protect against an attack of scarlet fever was obtained. But, as might be expected, the amount of toxin required to produce immunity, when administered by mouth, was many times the amount which produced comparable immunity when injected subcutaneously.

During the next several years, while experiments were being made to improve the method, immunization by mouth was limited to use in special cases, such as persons in whom hemophilia or severe cardiac lesions had been diagnosed or in institutions under quarantine for scarlet fever when speed in immunization was a prime consideration. It was also occasionally employed in highly susceptible individuals as a preliminary treatment to establish some immunity before hypodermic injections were begun, or in persons so highly sensitized to proteins contained in peptone that hypodermic injections of the toxin resulted in urticaria.

For obvious reasons, commercial distribution of undiluted fluid scarlet fever toxin in 1 liter volumes to be taken by mouth was not practical. It was apparent that it would be desirable to obtain the toxin in a more compact form and, if possible, in a dry state. To obtain such a preparation and to purify as well as concentrate the toxin for further chemical study, investigations were undertaken which have resulted in a highly concentrated and comparatively pure toxin in the form of a white powder.

This substance was carefully standardized, and weighed amounts were combined with pure saccharose to make powders containing different numbers of skin test doses of toxin. Given in these powders, the toxin caused more nausea and vomiting than when it was administered in the liquid state as crude toxin. We concluded that the reason for this difference was that the dry toxin remained in the stomach longer than when it was given in solution.

In an attempt to overcome this difficulty, the toxin was prepared in a saccharose syrup which the children found agreeable but which also caused more nausea than the hypodermic injections, though considerably less than the powders. Probably because of the loss of toxin through vomiting, the powders did not immunize. The syrup, causing less vomiting, produced satisfactory immunity.

In order to eliminate as far as possible nausea with resultant discomfort and sometimes loss of toxin, we decided to try protection of the toxin from absorption in the stomach. Enteric sealed capsules and enteric coated tablets were prepared. Of these two forms the tablets proved easier for small children to swallow. With the cooperation of one of the manufacturers, a number of enteric coated tablets were prepared from the purified toxin. These tablets were made in three strengths: a hundred thousand, one million and two million skin test doses per tablet.

There is considerable variation in the solubility of enteric coated tablets on the market. The solubility depends chiefly on four factors: the kind of substance used for the enteric coating, the thickness of coats applied, the rate of solution of the outer, decorative coat and the motility of the alimentary tract. In persons who have bowel movements at intervals of two or three days the chance of absorption is naturally better than in persons who eliminate residue of food in less than twenty-four hours after ingestion. We have found the standard chemical tests for solubility less satisfactory than actual feeding of the tablets under consideration along with an insoluble tablet, to serve as a marker, to persons known to have a habit of rapid elimination, and searching the stool which contains the marker for other undissolved tablets.

The use of tablets which do not dissolve prevents immunization, while the feeding of tablets that permit release of toxin in the stomach results in vomiting such as occurred when the powdered toxin was introduced directly into the stomach.

Tablets have been employed in the immunization of 131 persons susceptible to scarlet fever. With the exception of one case in this series, the reactions have not been recorded by us but by doctors or nurses in immediate charge of the groups or individuals, and the charts returned when the work was completed. The largest single group comprises fifty-four students at Berea College, where the immunization was supervised by Dr. Armstrong.

Preliminary skin tests were made in every case, and the size and intensity of the reaction were recorded. The skin test was repeated two weeks after completion of the immunization with the exception of one small group which there was no opportunity to retest until two months had elapsed. In the retests, one skin test dose of toxin was injected on the right forearm and two skin test doses on the left forearm. The immuni-

Read in the panel discussion on Some Contagious Diseases before the Section on Pediatrics at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Dick, George F., and Dick, Gladys Henry: Antitoxic Immunity Resulting from Administration of Toxin by Mouth, J. A. M. A. 98:1436 (April 23) 1932.

zation is not considered complete unless the cutaneous reaction to two skin test doses of toxin is negative at the time of retest shortly after completion of the doses.

Preliminary experiments directed toward determining the effective dosage indicated that, while some persons became immune with smaller amounts, the average total dosage should approximate seventy-five million skin test doses of toxin given over a period of three weeks. The tablets were taken immediately after meals, beginning, in most cases, with one hundred thousand skin test doses and gradually increasing to six or ten million skin test doses a day for the last three to six days. No modification of dosage was made on account of age. The series included individuals from 1 to 36 years of age.

In twelve persons the dosage was not carried above one to four million skin test doses a day. All but two in this group showed modified but positive cutaneous reactions on retest.

One group received improperly coated tablets which would partially dissolve in the stomach. In this group, vomiting and diarrhea were frequent complaints. Of the seventeen who completed the course of tablets, eleven, or 64.7 per cent, were immunized. Those who complained of diarrhea, so that they were less apt to absorb the toxin, acquired the least immunity.

Of the 102 persons of various ages who received better toxin tablets in amounts ranging from forty-seven to ninety-one million skin test doses distributed in graduated amounts over a period of two to three weeks, 94.7 per cent were immune on retest. In four cases, or 3.8 per cent, transient scarlatinal rashes occurred at some time, usually on the day four million skin test doses of toxin were given. Two persons vomited once.

With the more gradual increase in dosage in use during the past six months, and stricter control of the solubility of the tablets, reactions have been reduced to an occasional "stomach-ache" of short duration.

The series includes six persons who were so highly sensitized to the proteins contained in peptone that hypodermic injections were considered inadvisable. Their immunization by mouth was successful and uneventful. The further observation was made that, during the course of oral immunization, they became at least partially desensitized to peptone.

Results of further clinical experiments have shown that, whatever type of enteric coating is used, it is necessary to regulate the dosage of scarlet fever toxin according to the rate of disintegration or solution of the tablet. Immunization may be accomplished with doses of toxin smaller than those employed in the first experiments. In instances in which enteric coatings that permitted disintegration of the tablets within three hours in physiologic solution of sodium chloride buffered at p_H 7.0 were employed, the maximum daily dosage required to produce immunity was reduced to one to three million skin test doses of toxin.

It is not suggested that oral administration of toxin be generally substituted at this time for the present method of shallow hypodermic injections of sterile toxin in graduated doses. There are, however, definite advantages in the oral route in the conditions mentioned in the first part of this paper, the additional advantage that it lends itself more readily to modification according to the reactions of the individual patient and that immunization may be accomplished in a shorter time with fewer reactions.

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INTRAVENOUS USE OF 2-METHYL-1,4-NAPHTHOQUINONE IN HYPOPROTHROMBINEMIA

CLINICAL OBSERVATIONS

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AND
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The isolation and synthesis of vitamin K_1 (2-methyl-3-phytyl-1,4-naphthoquinone) in August of 1939 by Fieser and his associates,[1] by Doisy and his co-workers [2] and by Almquist and Klose [3] gave new impetus to the clinical evaluation of the antihemorrhagic activity of synthetic vitamin K_1 and its chemical derivatives in hypoprothrombinemia. It has been amply established by Ansbacher and his associates [4] and by others [5] that 2-methyl-1,4-naphthoquinone and more recently that 2-methyl-1,4-naphthohydroquinone are more rapidly acting and have greater potency than the many other derivatives of vitamin K_1 thus far elaborated in the biochemist's laboratory.

It is our purpose in this paper to report our experience with the intravenous use of 2-methyl-1,4-naphthoquinone for patients suffering from hypoprothrombinemia.

CHEMISTRY

Numerous chemical compounds closely related to the naturally occurring vitamin K_1 of alfalfa and K_2 of putrefied fish meal have been made available for clinical research, and certain facts have been established. Those compounds containing the phytyl group are less rapidly utilized by the animal's body.[6] The hydroxy group in the 3 position appears to reduce potency,[7] while the methyl group in the 2 position has been found essential. 2-methyl-1,4-naphthoquinone is a canary yellow crystalline substance, readily soluble in oil and slightly soluble in warm water (1 mg. in 10 cc.). The solution slowly loses potency on exposure to light but retains its activity in a dark refrigerator for several days. We have used 2-methyl-1,4-naphthoquinone exclusively in this study.

TOXICITY

Molitor and Robinson [8] determined the acute and chronic toxicities of 2-methyl-1,4-naphthoquinone on mice, rats and chicks. They found a very large safety

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2. Binkley, S. B.; Cheney, L. C.; Holcomb, W. F.; McKee, R. S.; Thayer, S. A.; MacCorquodale, D. W., and Doisy, E. A.: The Constitution and Synthesis of Vitamin K1, J. Am. Chem. Soc. **61**: 2558-2559 (Sept.) 1939.

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TABLE 1.—*Response to Treatment*

Case	Diagnosis	Jaundice	Bleeding	Liver Function	Dose of 2-Methyl-1,4-Naphthoquinone	Prothrombin Time in Percentage of Normal: Before Treatment	After Treatment: 2 Hr.	4 Hr.	6 Hr.	12 Hr.	1 Day	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	8 Days	9 Days	10 Days	Results
1	Portal cirrhosis; subacute yellow atrophy	+	+	80% retention of bromsulphalein Takata-Ara +	2 mg.	67	55	59	73	..	53 Died	..	..	..	..	..	..	..	..	..	Poor; very slight effect from oral or intravenous medication
2	Idiopathic steatorrhea	—	—		1 mg. repeated in 24 hours	62	65	..	..	..	63 Dose repeated	71	100*	..	..	..	..	..	..	..	Good response to 2d mg. dose
3	Carcinoma of head of pancreas	+	—		1 mg. repeated in 24 hours	50	68	70	74	72	78 (21 Hr.) Dose repeated	80 (45 Hr.)	100 (65 Hr.) Operation	..	..	..	* Transfusion	..	..	..	Good response to 2d mg. dose
4	Biliary fistula	+	+		1 mg.	10	..	..	..	100* (18 Hr.)	..	..	..	..	..	..	..	..	..	..	Good (child)
5	Common duct stenosis; biliary cirrhosis	+	+		1.5 mg. followed in 24 hr. by 1 mg. followed in 16 hr. by 2 mg.	33	..	..	..	66 (18 Hr.)	77 Dose repeated	58 Dose repeated	Died	..	..	..	..	..	..	..	Poor
6	Carcinoma of bile ducts	+	—		1 mg. repeated in 24 hours	55 Operation	..	..	..	73 (16 Hr.)	87 Dose repeated	100 (41 Hr.)	..	..	100	..	..	..	..	..	Good
7	Cirrhosis; common duct stone	+	—	Takata-Ara +	2 mg. followed in 24 hr. by 1 mg.	54	44	..	61	..	Dose repeated	Died	..	..	..	..	..	..	..	..	Poor
8	Common duct stone	+	—		2 mg.	95 Operation	100	100	..	..	..	..	100	..	..	100	..	..	..	..	Good; prothrombin maintained
9	Biliary fistula	+	—		2 mg.	49	64	73	..	80 (13 Hr.)	100	105 (36 Hr.)	Operation, transfusion	93	..	83	..	..	71*	..	Good
10	Biliary fistula; hepatitis	+	+	Hippuric acid less than 0.44 Gm.	2 mg. repeated in 10 days	62 55 Bleeding	90 62	90 70	.. ..	100 ...	.. 70	.. 82*	Operation	100 ...	... 100	.. ..	83 Transfusion	.. ..	.. ..	.. ..	55† Good first response; delayed 2d response after hepatitis developed
11	Carcinoma of hepatic flexure of colon with obstruction	—	+		2 mg.	72 Operation	86 (1½ Hr.)	..	..	100 (15 Hr.)	..	..	..	90	..	..	Transfusion	88*	..	..	Good
12	Jejunal fistula	—	+		2 mg. repeated in 5 days	49	..	..	81 (7 Hr.)	..	100 (23 Hr.)	..	..	94	70 Dose repeated	..	..	..	..	..	Good
13	Hepatitis	+	—		2 mg. repeated in 2 days	80	88	88	..	..	..	80 Dose repeated	..	..	..	86	..	..	..	73*	Fair
14	Biliary fistula	—	+		2 mg.	83	83	87	87	..	95	..	100*	..	..	..	..	..	..	..	Good
15	Carcinoma of gallbladder; biliary fistula; biliary cirrhosis	+	—		2 mg. repeated in 6 days	58	..	..	..	60	..	60*	..	..	..	60 Dose repeated	..	85	..	..	Fair after 2d dose
16	Biliary obstruction by duodenal ulcer	+	—		2 mg.	90 Operation	..	..	100	..	..	98	..	100	..	..	..	..	..	..	Good; prothrombin maintained
17	Common duct stricture; biliary cirrhosis	+	+		2 mg. repeated in 4 days	40	52	..	76	81	80 26 Hr.	91	86	76 Dose repeated	91	..	87	..	..	87	Good but level not maintained
18	Common duct stricture	+	—		2 mg.	76	..	..	76	..	90	100*	..	Operation	..	..	..	..	..	..	Good
19	Common duct stone	+	—		2 mg.	76	..	..	..	80	100 1½ days	..	..	..	..	..	..	..	..	..	Good
20	Gastric ulcer; subtotal gastrectomy	—	+		2 mg.	76	..	..	..	92	103	84	..	..	..	..	..	..	..	..	Good
21	Cirrhosis; carcinoma of rectum	—	—		2 mg.	70	..	..	..	66 10 Hr.	94 28 Hr.	94*	..	..	..	..	..	..	..	..	Good; slower than usual
22	Carcinoma of head of pancreas	+	—		2 mg.	72	..	..	..	77 19 Hr.	100* 28 Hr.	..	..	..	..	..	..	..	..	..	Good

* Oral medication begun.
† Dose repeated.

factor between the toxic and therapeutic doses; 500 mg. per kilogram of body weight was the L. D. 50 orally in mice with this substance. Chronic toxicity in rats was tested over a period of thirty consecutive days on varying daily doses; 500 mg. per kilogram of 2-methyl-1,4-naphthoquinone was toxic and 350 mg. per kilogram caused a marked fall in red blood cell count and

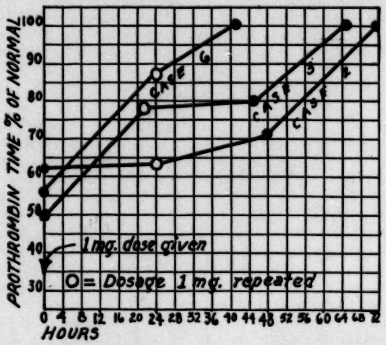

Chart 1.—Effect of 1 mg. intravenous doses of 2-methyl-1,4-naphthoquinone on hypoprothrombinemia.

in hemoglobin. Natural vitamin K_1 did not cause these changes.

In the human being no toxic effect from 2-methyl-1,4-naphthoquinone has been reported when small oral doses were used, but Koller [9] has described nausea and vomiting following the oral administration of large doses (3 mg. per kilogram of body weight).

METHOD

In this study we have used Quick's [10] method of prothrombin time determination but have reported this

TABLE 2.—*Conditions Considered Most Important in Causing Hypoprothrombinemia*

	Cases
Common duct obstruction	8
Biliary fistula	4
Cirrhosis	4
Hepatitis	1
Subacute yellow atrophy	1
Idiopathic steatorrhea	1
Subtotal gastrectomy	1
Jejunal fistula	1
Obstruction of large intestine	1
	22

in terms of percentage of normal as suggested by H. J. Perkin of the clinic's research laboratory early in our investigation of vitamin K and related prothrombogenic substances. This method permits minor changes in potency of the thromboplastic substance without affecting the final result in the individual test. The patient's prothrombin time in percentage of normal is calculated by dividing the patient's prothrombin clotting time by the normal control's prothrombin clotting time and multiplying by 100.

9. Koller, F.: Ueber die klinische Wirksamkeit von Naphtochinonderivatin (Vitamin K-Wirkung), Schweiz. med. Wchnschr. **69**: 1159-1161 (Nov. 11) 1939.

10. Quick, A. J.; Stanley-Brown, M., and Bancroft, F. W.: Study of Coagulation Defect in Hemophilia and in Jaundice, Am. J. M. Sc. **190**: 501-511 (Oct.) 1935.

Prothrombin determinations were made immediately before intravenous treatment was administered and at varying intervals thereafter. We have considered a prothrombin clotting time of 90 per cent or over as normal.

The solution of crystalline 2-methyl-1,4-naphthoquinone [11] was prepared by dissolving 10 mg. in 100 cc. of sterile hot physiologic solution of sodium chloride. This was used immediately or was protected from light and stored for short periods of time in the refrigerator. The intravenous injection was made slowly into an antecubital vein.

RESULTS

During the seven months between February and September of 1940 we have administered 2-methyl-1,4-naphthoquinone intravenously to twenty-two patients, twenty of whom had hypoprothrombinemia. A brief outline of these cases, together with their response to treatment is presented in table 1. The conditions considered most important in causing the hypoprothrombinemia in each case have been summarized in table 2. Patients 8 and 16 received 2-methyl-1,4-naphthoquinone prophylactically. The response to intravenous treatment was considered good in 17 (77.3 per cent), fair in 2 (9.1 per cent) and poor in 3 (13.6 per cent).

In attempting to establish the minimum effective intravenous dose of 2-methyl-1,4-naphthoquinone in the adult it was demonstrated that although 1 mg. would usually cause a definite rise in the prothrombin level a second milligram dose was needed before a normal prothrombin could be obtained. Patient 4 showed a complete response to 1 mg. intravenously, but this

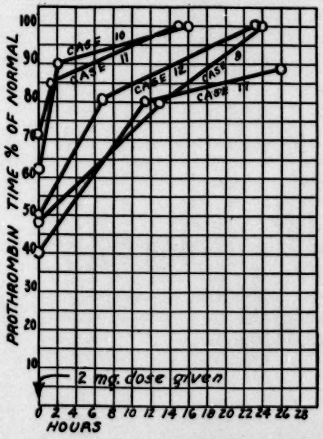

Chart 2.—Effect of 2 mg. intravenous dose of 2-methyl-1,4-naphthoquinone on hypoprothrombinemia.

patient was a 3 year old child. Chart 1 demonstrates the limitation of response to the 1 mg. dose in the adult.

The effect of a 2 mg. dose of 2-methyl-1,4-naphthoquinone intravenously is shown in chart 2. These patients were selected to demonstrate this point because of their initial low levels of prothrombin and because liver damage, with the exception of case 17, was absent or of such degree as not to interfere seriously with the

11. The crystals were supplied to us by E. R. Squibb & Sons.

response. From these results we conclude that some patients may be expected to show beginning effect as early as two hours after receiving intravenous medication, that a prothrombin level of 80 per cent of normal is reached in an average of about seven and one-half hours, and that 100 per cent of normal is attained in an average of about twenty hours.

The duration of the effect of 2 mg. of 2-methyl-1, 4-naphthoquinone is shown in chart 3. It is seen that the prothrombin level will remain above 90 per cent of normal for four or more days unless complicated by liver damage. Case 17, in which there was some liver impairment, also appears on the chart and shows a more rapid drop.

We have confirmed the reports of numerous other investigators with regard to the effect of liver damage and have found no increased response in such cases by the intravenous route of administration as compared with the oral route. The patients who responded slowly or incompletely suffered, without exception, from

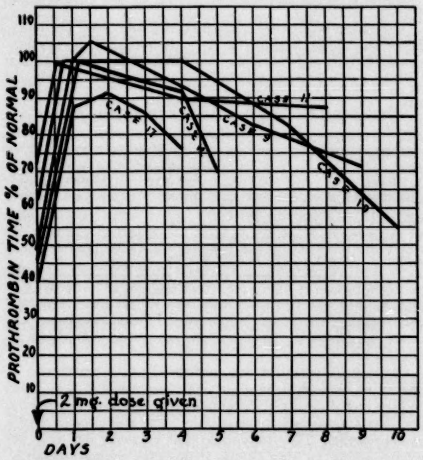

Chart 3.—Duration of effect after 2 mg. intravenous dose of 2-methyl-1,4-naphthoquinone on hypoprothrombinemia.

some degree of liver damage. This was demonstrated in some cases by liver function tests and in others by direct observation of the liver at operation. Severe liver damage was necessary to prevent more than a slight response to intravenous 2-methyl-1,4-naphthoquinone (cases 1 and 7). When the impairment of liver damage was less severe, some initial increase in prothrombin occurred but the response was not complete and the prothrombin clotting time could not be lowered to a completely normal level nor could it be maintained as easily as in those cases in which there was no appreciable liver damage (cases 5, 10, 13, 15, 17 and 21). Repeated intravenous doses in this group sometimes led to more normal levels (case 15).

In nine cases bleeding occurred before the administration of 2-methyl-1,4-naphthoquinone, but bleeding was effectively controlled except in cases 1 and 5, in which severe liver damage existed.

By this route of administration bile salts were not necessary.

Except for the temporary pain near the site of injection in five cases, no toxic effects were noted. In no case could any drop in blood count or hemoglobin level be attributed to this drug.

REPORT OF CASES

We have chosen four illustrative cases to present in detail:

CASE 1.—A man aged 43, a druggist, entered on Jan. 23, 1940, with a story of recurrent jaundice of two years' duration. He had been a heavy drinker for three years before the onset of this condition but had consumed no alcohol in the two years previous to entry. There had been no pain, chills or fever. Roentgenograms taken elsewhere two weeks before entry were said to show a stone in the gallbladder region. Slight epistaxis had occurred occasionally, as well as some bleeding from the gums.

Physical examination showed the scleras to be slightly icteric. The skin was dry and there were a few follicular keratoses on the arms. On the lower legs were several papular, purpuric, pin point lesions. The liver extended from the sixth interspace superiorly to a sharp edge 3 fingerbreadths below the right costal margin. It extended well into the epigastrium and was smooth, firm and slightly tender. The splenic tip descended 2 fingerbreadths below the left costal margin. No ascites could be elicited. There were numerous dilated venules over the lower anterior chest wall bilaterally. There was no peripheral edema.

The patient was sent immediately into the hospital with the diagnosis of biliary cirrhosis and a question of cholelithiasis. Laboratory test showed 15.6 Gm. of hemoglobin (100 per cent Sahli), 5,000,000 erythrocytes and 6,330 leukocytes. The prothrombin time was 65 per cent; the bilirubin showed an indirect reaction and was 2.8 mg. per hundred cubic centimeters. The urobilinogen was positive in 1:256 dilution. The serum protein was 7.5 per cent, the Hinton test was negative and the urine was normal. The icteric index was 45. The Takata-Ara test was strongly positive and 80 per cent of the bromsulphalein was retained after one hour.

The patient was given vitamin B complex by mouth and members of the B complex intramuscularly. He was given 2-methyl-1,4-naphthoquinone orally in 2 mg. doses three times a day, together with bile salts 10 grains (0.65 Gm.) three times a day. At the end of nine days the prothrombin had risen to 75 per cent and at this time natural vitamin K_1 was given orally with bile salts, without any further rise in the prothrombin time.

In spite of the evidence of hepatitis and our inability to raise the prothrombin time to a normal level, an exploration was deemed necessary. This was done February 10. A markedly scarred liver was found, but no stones were felt. The liver biopsy showed a toxic hepatitis with cirrhotic changes.

The patient did poorly after operation. His prothrombin dropped to 53 per cent of normal, and oral 2-methyl-1,4-naphthoquinone, together with bile salts, raised this to 67 per cent of normal.

On the seventh postoperative day the patient began to show evidence of cholemia and uremia and vomited a total of about 6 ounces (178 cc.) of blood. His prothrombin time was 67 per cent of normal, and 2 mg. of 2-methyl-1,4-naphthoquinone was given intravenously. The poor prothrombin response is shown in table 3.

The patient died on the eighth postoperative day. Postmortem examination showed toxic cirrhosis of the liver with a superimposed subacute yellow atrophy, massive gastrointestinal hemorrhage and cholelithiasis with soft stones in the bladder but none in any of the ducts.

CASE 4.—A boy aged 3 years was brought to the clinic on Jan. 31, 1940, because of an abdominal mass present since the age of 12 months and jaundice of two weeks' duration. The parents had been told that the abdominal mass was an enlarged liver. There had been several attacks of cough, anorexia, clay-colored stools, dark urine and general malaise. During these attacks the abdominal mass increased in size, but as the symptoms subsided the mass became smaller and the color of the

stools and urine returned to normal. Jaundice had been present for about two weeks before admission and there had been a mild pruritus for several days.

On physical examination the boy was well developed and well nourished, with moderate pallor of the mucous membranes and a mild icterus of the scleras. There were a few excoriations on the skin of the trunk and legs. A few medium rales were heard throughout both lung fields. Examination of the abdomen revealed a cystic mass approximately 9 cm. in diameter in the right half of the abdomen. The spleen was not palpated. A few shotty cervical glands were felt. The temperature was 99 F. by rectum, the weight 35½ pounds (16 Kg.) and the height 39½ inches (100 cm.). The rest of the physical examination gave essentially normal results.

TABLE 3.—*Prothrombin Response in Case 1*

Date	Prothrombin Time, per Cent	2-methyl-1,4-naphthoquinone
2/17/40 8:45 a. m.	67	2 mg. intravenously
10:30 a. m.	55	
12:30 a. m.	59	
2:45 p. m.	73	
4:30 p. m.	67	
2/18/40 a. m.	55	

The urine on admission showed a trace of bile but was otherwise negative. The bile gradually increased in the urine after entry, the leukocyte count was 11,450, hemoglobin 62 per cent (Sahli), erythrocytes 4,080,000, differential 80 per cent polymorphonuclears, 17 per cent lymphocytes, 3 per cent monocytes. The icteric index was 17 and the hematocrit reading 40. The bilirubin was 1.4 mg. per hundred cubic centimeters. The platelet count was 544,000, the reticulocyte count 1.9 per cent. There was moderate achromia. The stools showed a trace of bile.

After a mild bronchitis had cleared, exploratory operation was performed on February 15. At this time a congenital dilatation of the common bile duct, containing about a liter of bile, was found, and marsupialization of the dilated duct was carried out. The prothrombin clotting time preoperatively was 100 per cent of normal and remained so immediately after operation. Large amounts of bile drained through the catheter which had been placed in the common bile duct and an attempt was made to give the patient bile salts by mouth. This was only partially successful, as he refused this medication on and after March 13. On March 18 the urine began to show many red blood cells in the sediment. On March 21 he became nauseated and vomited several times, was listless and had a fever of 101 F. by rectum in the evening. A hypodermoclysis was given on this date and there was some bleeding from the skin wounds after the withdrawal of the needles. The next day, March 22, he bled from the needle wound in the lobe of the ear where blood had been taken. On March 23 bright red blood was passed by rectum and the bleeding continued from the ear lobe and from the nose.

TABLE 4.—*Prothrombin Response in Case 9*

Date	Prothrombin Time, per Cent	2-methyl-1,4-naphthoquinone
5/18/40 9:00 p. m.	49	2 mg. intravenously
10:00 p. m.	51	
11:00 p. m.	64	
12:00 m.	73	
5/19/40 10:15 a. m.	80	
8:00 p. m.	100	
5/20/40 8:00 a. m.	105	

Examination of the blood at this time showed a leukocyte count of 16,000, and the hemoglobin had dropped from 89 per cent on March 1 to 60 per cent. The prothrombin clotting time on March 23 was found to be 10 per cent of normal. At 5 p. m. 1 mg. of 2-methyl-1,4-naphthoquinone, dissolved in 10 cc. of physiologic solution of sodium chloride was given intravenously. By 7 o'clock the same evening all bleeding had stopped, and eighteen hours after the medication the prothrombin time was 100 per cent of normal.

The patient's clinical condition improved markedly, his temperature fell to normal, his appetite returned and he was again running about the wards. He was then given tiny repeated doses of bile salts and 6 mg. of 2-methyl-1,4-naphthoquinone orally each day. The prothrombin time remained 100 per cent of normal. On March 30, choledochoduodenostomy was performed. The patient was discharged on April 13, with normal colored stools and urine, and with all evidence of jaundice gone.

CASE 9.—A man aged 42, a druggist, admitted on May 17, 1940, had had attacks of epigastric pain during the previous year extending to the right scapular region. Three weeks before entry he had undergone a cholecystectomy elsewhere, at which time several stones were removed. Following this procedure he had become intensely jaundiced, had experienced chills and fever, and had noted dark urine and light colored stools. One week before entry a biliary fistula had developed and the jaundice had partially subsided.

Physical examination was essentially negative except for moderate icterus of the skin and scleras, a palpable liver edge 1 fingerbreadth below the right costal margin and a biliary fistula.

The patient entered the hospital on the same day. The icteric index was 35, the hemoglobin 91 per cent (Sahli), the erythrocytes 5,010,000 and the leukocytes 5,500. The serum bilirubin was 7.8 mg. per hundred cubic centimeters (indirect). May 18 at 9 p. m. the prothrombin time was 49 per cent of normal and at this time 2 mg. of 2-methyl-1,4-naphthoquinone was given intravenously. His prothrombin response is shown in table 4.

TABLE 5.—*Response to 2-Methyl-1,4-Naphthoquinone in Case 10*

Date	Prothrombin Time, per Cent	2-methyl-1,4-naphthoquinone
5/19/40 3:30 p. m.	62	2 mg. intravenously
4:30 p. m.	63	
5:30 p. m.	90	
6:30 p. m.	90	
7:30 p. m.	90	
5/20/40 8:00 a. m.	100	

On May 21 operation was performed and a transfusion of 500 cc. of citrated blood given. The common duct was found to have been divided and the intrahepatic portion of the common duct was anastomosed to the jejunum. The postoperative course was uneventful. The prothrombin time gradually fell to 71 per cent of normal on May 27, and at this time natural vitamin K_1 and bile salts were started by mouth. On June 6 the prothrombin time had risen to 89 per cent. The patient was discharged markedly improved on June 9, at which time his icteric index was 9 and the bilirubin 0.1 mg. per hundred cubic centimeters (indirect).

CASE 10.—A woman aged 31, a housewife, entered the clinic on May 18, 1940, complaining of the presence of a bile fistula of five months' duration. She had had a cholecystectomy elsewhere in 1931 and in November of 1939 had had a recurrence of right upper quadrant pain. In January 1940 another operation was performed elsewhere and she was told that her common bile duct had "shriveled up." A T tube had been sutured in place and was there on admission to the hospital. At this time there was slight bleeding around the tube.

On physical examination the patient appeared thin and jaundiced and was in no acute distress; she showed general malnutrition and tenderness in the right upper quadrant, where there was a rubber catheter in place.

She entered the hospital immediately and there a urine examination revealed albumin 3+ and bile 2+. The bilirubin was 9.0 mg. per hundred cubic centimeters, the nonprotein nitrogen 21 mg. per hundred cubic centimeters. The leukocytes numbered 11,750, the erythrocytes 3,440,000; the hemoglobin was 66 per cent (Sahli). The differential was normal. The Hinton test was negative. Examination of the stools showed

a 3+ benzidine test for blood and no bile. The prothrombin time was found to be 50 per cent of normal.

The patient was given 2 mg. of 2-methyl-1,4-naphthoquinone intravenously, and the response is shown in table 5.

On May 22 the patient underwent operation, and a stricture at the ampulla of Vater was found. This was dilated and a T tube left in the common bile duct. Four days after operation the prothrombin had fallen to 83 per cent. At this time she was given a transfusion of 250 cc. of citrated blood and on the seventh postoperative day the prothrombin time had dropped to 55 per cent and she started to bleed. At this time she was given another 2 mg. of 2-methyl-1,4-naphthoquinone intravenously, and the prothrombin time was brought up to 83 per cent of normal in two days. All bleeding had stopped five hours after the medication had been given intravenously. At this time she was given natural vitamin K_1 and bile salts by mouth three times a day, and the prothrombin time rose to 100 per cent. On June 19 the T tube was removed. Following this a temperature of 102.4 F. developed and the bilirubin rose to 17.0 mg. per hundred cubic centimeters. On June 21 the prothrombin had dropped to 65 per cent and she again received 2 mg. of 2-methyl-1,4-naphthoquinone intravenously, but the prothrombin time remained low in spite of the fact that the dose of 2 mg. was repeated in twenty-four hours and 1 mg. in forty-eight hours. At this time an intravenous hippuric acid test was less than 0.44 Gm., thus showing marked liver damage, which was thought due to hepatitis.

The fever gradually subsided and the bilirubin dropped to 13 mg. per hundred cubic centimeters. The patient was given 2-methyl-1,4-naphthoquinone and bile acids by mouth. As the evidence of hepatitis subsided the prothrombin gradually rose to 90 per cent in the course of the next four days. She was discharged improved on June 28.

Case 1 demonstrates the ineffectiveness of 2-methyl-1,4-naphthoquinone when severe liver damage existed. Case 4 illustrates the dramatic effect of this drug in bleeding due to hypoprothrombinemia. In case 9 the average response of uncomplicated vitamin K deficiency to 2-methyl-1,4-naphthoquinone, given intravenously, is shown. Case 10 contrasts the effect of 2-methyl-1,4-naphthoquinone in hypoprothrombinemia before, during and after the development of liver impairment.

COMMENT

The value of the prothrombogenic chemicals in raising lowered blood prothrombin levels has been amply demonstrated. 2-methyl-1,4-naphthoquinone by the intravenous method of administration has proved highly effective. The minimum effective dose has been found to be 2 mg. for the adult. Although this dose has had a definite effect within two hours and has raised low levels to an entirely normal figure in twenty hours, it may well be that larger doses would result in earlier normal values and that the duration of effect might be substantially prolonged. Further investigation along these lines is to be desired. The possible prolongation of effect with greater doses depends largely on the ability of the body and especially of the liver to store prothrombin or its precursor, a point needing clarification.

Although severe liver damage appears necessary to prevent adequate elevation of the blood prothrombin after the intravenous injection of 2-methyl-1,4-naphthoquinone, lesser degrees of liver impairment appear to lead to a slower onset of response, a lessened height of response and a response of shorter duration. Under certain circumstances the application of these facts may be of definite value in determining the degree of impairment of one important liver function. We feel that transfusions should be delayed when possible until after the patient's response to the prothrombogenic substance has been determined in order that poor liver function may not be obscured. Patients who have been unable to raise their prothrombin to a normal level when 2-methyl-1,4-naphthoquinone has been given intravenously before operation have done poorly after operation.

While the intravenous mode of administration presents definite advantages under circumstances in which oral administration is not feasible, as in nauseated patients or when the most rapid effect is essential as in bleeding, we do not propose that this route be used in all cases, the oral method being considered simpler for the average patient. The instability of the aqueous solution of 2-methyl-1,4-naphthoquinone and the ease with which this chemical is precipitated from solution when chilled are disadvantages to its routine use.

As previously stated, we have considered any prothrombin figure 90 per cent or above as normal. We wish to stress the importance of attaining an entirely normal figure before surgery is attempted, since it is wise to know that a normal level can be reached or that liver damage prevents this response. Much prothrombin may be lost during operation because of blood loss, and this may cause the already lowered prothrombin to fall to a dangerous level. We have found that in some cases bleeding may occur with a prothrombin level as high as 70 per cent of normal, although this is true usually for patients with considerable liver damage and confirms the probability that other factors are involved in this bleeding.

SUMMARY

1. 2-methyl-1,4-naphthoquinone has been administered intravenously to twenty-two patients. It has proved to be efficient in raising the prothrombin level. Bile salts were not necessary for this response.

2. With the exception of local distress of short duration at the time of injection, no toxic manifestations have been observed.

3. The minimal effective intravenous dose of 2-methyl-1,4-naphthoquinone in the adult was found to be 2 mg.

4. In cases uncomplicated by liver impairment a 2 mg. dose given intravenously raised the prothrombin level from 50 per cent to 80 per cent in an average of seven and one-half hours and to 100 per cent in an average of twenty hours.

5. A 2 mg. intravenous dose kept the prothrombin level above 90 per cent of normal for four or more days unless liver damage was present.

6. Severe liver damage permitted only a slight response to intravenous 2-methyl-1,4-naphthoquinone. If liver impairment was less marked, the effect was manifested in a slower onset of response, a lessened height of response, and a shorter duration of response.

7. Bleeding was rapidly and effectively controlled unless severe liver damage was present.

8. The intravenous route of administration has great value in patients for whom oral administration is difficult or impossible, as well as in those cases in which rapid cessation of bleeding is imperative.

A Pilot May Faint.—Human physiology sets no definite speed limit, but, if you are going fast, turning is dangerous, because it drains the blood into the parts of the body on the outside of the turn and may cause fainting. In particular, if a pilot turns a rapidly moving aeroplane upwards, his blood is forced down into his legs, and he may faint.—Haldane, J. B. S.: Science and Everyday Life, New York, Macmillan Company, 1940.

ORTHOSTATIC HYPOTENSION AND ORTHOSTATIC TACHYCARDIA

TREATMENT WITH THE "HEAD-UP" BED

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Orthostatic hypotension is characterized chiefly by a sharp decrease in blood pressure when a patient afflicted with it stands. The blood pressure is ordinarily normal when the patient lies. If the blood pressure decreases to a low level, weakness and syncope result. Other relevant signs or symptoms are deficient sweating, either localized or generalized, secretion of larger amounts of urine when the patient is recumbent than when he is erect and in some cases a failure of the pulse rate to increase markedly when the patient assumes the erect posture. Orthostatic hypotension should be suspected whenever a patient has exhaustion in the morning which lessens during the day, whenever weakness, dimness of vision or syncope occurs on assumption of the erect posture and disappears on lying down, whenever episodes of syncope are inadequately explained and whenever there is diminished sweating. This condition has been considered by some to be the result of failure of adequate constriction of arterioles when patients stand.[1] The failure of the arterioles in turn has been assumed to result from a defect in the autonomic nervous system. This concept has been based on logical interpretations of clinical data: 1. Extensive sympathectomy in cases of essential hypertension results in a diminution of arteriolar tone which has seemed to explain the orthostatic hypotension which ordinarily results from extensive sympathectomy. 2. Drugs which increase arteriolar tone dramatically relieve the orthostatic symptoms and markedly improve the blood pressure in the erect posture.[2] The natural assumption followed that it is deficiency in arteriolar resistance which results in the low blood pressure when the patient stands. 3. The disturbances in sweating frequently found in cases of orthostatic hypotension have appeared to demonstrate a primary disturbance in the autonomic nervous system.[1] Hypofunction of this cholinergic part of the autonomic nervous system seemed an index of a similar disturbance in the adrenergic portion of the autonomic nervous system which resulted in a loss of arteriolar tone.

Recent studies, which we are not presenting in detail in this paper, suggest that the defect in postural adaptation is not a defect in arteriolar vasoconstriction but rather one in the maintenance of adequate return of venous blood to the heart. The evidence in brief may be summarized as follows: 1. Weiss and his associates have shown that circulatory collapse may be induced by the erect posture when normal subjects are given appropriate amounts of sodium nitrite.[3] Syncope produced by this artificial method appears to be the result of the loss of venous tone and the pooling of blood in the dependent portions of the body and closely resembles the syncope observed in cases of orthostatic hypotension. 2. We have been able to demonstrate a deficient "potential" in the venous return to the heart in all cases of orthostatic hypotension which we have studied by the Flack test, which consists in having the patient blow against the column of mercury of a sphygmomanometer with the glottis open.[4] The resulting increase in intrathoracic pressure increases the resistance which the venous blood has to overcome in traveling back to the right side of the heart and is a measurement of the potential of the venous return. Normal subjects can maintain the mercury column at 40 mm. of mercury for periods of at least twenty-five seconds, with little change in pulse rate or blood pressure. Patients with orthostatic hypotension become pulseless and collapse within a period of ten seconds. Fluoroscopic and roentgenographic studies of the heart show a diminution in the size of the heart and great vessels during this period of increased intrathoracic pressure (fig. 1). However, when these patients are placed in a recumbent position with the head 30 degrees lower than the feet, the Flack test approaches normal in some cases. 3. The temperature of the skin of the toes and of the fingers of two individuals with orthostatic hypotension changed in a normal fashion in response to different environmental temperatures and to application of heat to the trunk. These studies indicate that the peripheral arterioles respond normally by dilatation and constriction in a reflex manner to changes in temperature. The autonomic innervation of the arterioles seemed, therefore, to be intact functionally.[5] 4. In cases of orthostatic hypotension the peripheral arterioles offer adequate resistance to maintain the blood pressure at normal levels when the patient is recumbent. It seems illogical that simple assumption of the erect posture could cause loss of arteriolar tone. 5. The arteriolar vasoconstricting substances ephedrine, epinephrine, paredrinol (racemic parahydroxy-α,N-dimethylphenethylamine) and amphetamine raise the whole level of blood pressure in cases of orthostatic hypotension, but use of them does not prevent the abnormal decrease in blood pressure when patients stand.

These five observations suggest that there is no deficiency in arteriolar tone in the syndrome of orthostatic hypotension but rather that there is a diminution in the maintenance of adequate return of venous blood to the heart, which results in a diminished cardiac output and a decrease in the arterial blood pressure when patients stand.

ORTHOSTATIC HYPOTENSION

An attempt to find a remedy for orthostatic hypotension in the field of vasoconstricting drugs has proved in our hands disappointing. We have used ephedrine,

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Read before the Section on Pharmacology and Therapeutics at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

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5. Fatherree, T. J., and Allen, E. V.: Sympathetic Vasodilator Fibers in the Upper and Lower Extremities: Observations Concerning the Mechanism of Indirect Vasodilatation Induced by Heat, Arch. Int. Med. **62**: 1015-1028 (Dec.) 1938.

paredrine (parahydroxyphenylisopropylamine), prostigmine methylsulfate and guanidine hydrochloride. These substances have given symptomatic relief and they have prevented the reduction of blood pressure to a low level when patients stand. However, in two cases which we studied carefully the beneficial results were only temporary.

During investigation of the value of various therapeutic procedures, we noted that patients with orthostatic hypotension appeared to improve symptomatically and objectively during the daytime and that this improvement had disappeared in the morning after sleep in bed at night. The implication in this observation was that these patients lost some of their ability to adapt themselves to changes in posture as the result of either sleep itself or as a result of the recumbent position in which they slept. This observation led to the suggestion that patients with orthostatic hypotension should not sleep in a flat bed but should lie in a semi-inclined or "head-up" position[6] (fig. 2). The results of this type of treatment have been so startling that we are reporting illustrative cases. The following is a case of spontaneous orthostatic hypotension:

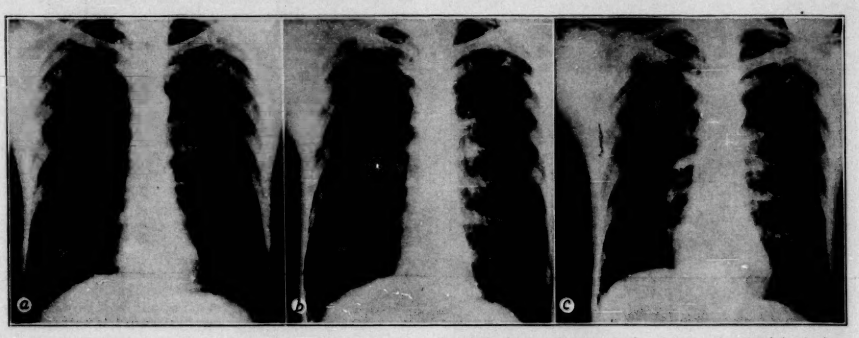

Fig. 1.—Evidence of the effect of increased intrathoracic pressure on size of the heart and great vessels: (*a*) control; normal inspiration; (*b*) Flack test of 40 mm. of mercury at the end of five seconds; (*c*) expiration at the completion of the Flack test.

A man aged 59 first registered at the Mayo Clinic July 5, 1939. He complained of dizziness, blurring of vision, exhaustion and syncope associated with standing erect. These symptoms had begun insidiously a year prior to registration and had progressed to the point of severe disability. He was unable to walk more than two blocks without resting. He presented the typical features of spontaneous orthostatic hypotension. The recumbent blood pressure in millimeters of mercury was 130 systolic and 80 diastolic; at the end of one minute of standing it was 70/40. At the end of five minutes of standing the blood pressure was 55/45. The heart rate did not increase when the patient stood. The Flack test gave positive results. When the patient blew the mercury column to the 40 mm. mark, syncope resulted at the end of five seconds. When the patient was in the recumbent position and was tilted with the head down at an angle of 30 degrees, he was able to blow the mercury column to the 50 mm. mark and retain it there for a period of twenty-two seconds without syncope. Roentgenoscopic and roentgenologic studies of the heart during the periods of increased intrathoracic pressure showed diminution in the size of the heart and in the size of the great vessels in the mediastinum when the patient blew against a column of mercury. The administration of prostigmine methylsulfate subcutaneously resulted in improvement in the subjective symptoms. When the patient stood his blood pressure was higher than before the drug was given. Guanidine hydrochloride given orally was even more beneficial and on this medication he remained free from symptoms for a week. At the end of this time both prostigmine and guanidine appeared to lose their effect, and the patient reverted to his former condition. Medication with ephedrine and amphetamine was only temporarily beneficial. The patient's condition became steadily worse and for a period of three months prior to his last examination he was confined to bed and to a wheel chair.

The patient returned to the clinic March 25, 1940. The orthostatic hypotension had greatly increased. Several determinations of blood pressure with the patient recumbent averaged 130/80. The patient was unable to stand erect for longer than three minutes because of syncope which then occurred. The blood pressure at the end of one minute of standing in the erect posture could not be obtained. The patient was unable to sweat over the face, trunk and extremities when his body was subjected to radiant heat. Paredrinol, prostigmine methylsulfate, epinephrine and guanidine hydrochloride did not significantly change the blood pressure when the patient was erect or alleviate the patient's disability (fig. 3).

The patient was then placed in a bed the head of which was elevated 18 inches. During the daytime he was encouraged to sit in a chair. Improvement occurred quickly. The patient was able to stand erect for longer and longer periods. He became more active and was capable of walking for short distances. At the end of four days of this treatment the patient was able to stand erect for periods longer than an hour without syncope. When he stood the blood pressure slowly fell from 100/60 to 60/40 at the end of an hour (fig. 4). Previously the best effect of treatment was ability to stand ten minutes following the injection of epinephrine (fig. 3). The improvement could be made to disappear, for when the patient slept one night in a level bed the blood pressure on the following morning when he was in the erect posture could not be obtained and syncope occurred within one minute.

The patient has continued to sleep on the tilted bed since that time. Within two weeks he went to work for the first time in seven months. Two months after treatment on the tilted bed had been begun he had not had an attack of syncope. At present he works six hours a day in his office and two hours a day in his garden. He has recovered his ability to sweat over his face, arms and trunk. He is not, however, cured of vascular disability, for he still has orthostatic hypotension. In the erect posture the blood pressure still decreases to 60/40 at the end of an hour, but he has recovered a measure of postural vascular adaptability sufficient to allow him to function in a comparatively normal fashion. We do not pretend that the tilted "head-up" bed alone has been responsible for this improvement. It has been instrumental in preventing the loss of postural

6. The term "head-up" will be used in this paper to designate a position accomplished by placing the posts of the head of a bed on ordinary kitchen chairs or on chairs of similar height, that is, about 18 inches. Patients sleep comfortably in this position, although some may need a hard pillow under the mattress at the level of the thighs to prevent slipping.

vascular adaptability which the patient gained during the daytime and which previously he had been losing by sleeping on a flat bed.

The following case is one of orthostatic hypotension induced by sympathectomy for essential hypertension:

A woman aged 34 had an extensive sympathectomy performed May 28, 1940, because of essential hypertension. June 6 a similar operation was performed on the left side. June 24 the blood pressure decreased from 160/110 when she lay to 60/40 after standing for forty-five seconds, at which time she became so weak that she was forced to lie again to prevent syncope. The pulse rate increased from 94 per minute on lying to 140 when she stood. For three days she slept on the "head-up" bed at night and sat in a chair or walked a little during the day. At the end of this period she could stand or walk without weakness or syncope. She felt entirely well and she was able to stand for thirty minutes without symptoms. The blood pressure when lying was 130/100 and her pulse rate 70 per minute. The blood pressure when she stood was 150/100 and the pulse rate was 100. For the next twenty-four hours the patient slept on a horizontal bed at night and continued as active as her strength permitted during the day. The blood pressure while lying in bed then was 144/110 and the pulse rate 78. She could stand for only forty-five seconds because of weakness. The systolic blood pressure at the end of this time was 50 mm. of mercury and the diastolic blood pressure could not be determined. The pulse rate was 130 per minute. During the next

Fig. 2.—The tilted "head-up" bed.

day she rested or slept on the "head-up" bed or rested in a chair. At the end of this period when she lay in bed the patient's blood pressure was 148/112 and her pulse rate was 90. At the end of five minutes of standing the blood pressure was 96/70 and the pulse rate 138. She felt better than she had on the day before but did not feel entirely well. The patient continued to sleep or rest on the "head-up" bed for two days and her condition continued to improve. At the end of this time, the respective values for blood pressure and pulse when she lay were 140/112 and 72. After five minutes of standing they were 146/110 and 124. She felt entirely well. During a subsequent period of twenty-four hours she slept or rested on a horizontal bed. At the end of this time she was unable to stand for a minute because of syncope. The blood pressure was indiscernible and the pulse rate increased to 150 per minute just before she fainted.

Study of the patient demonstrated unequivocably that resting and sleeping on the "head-up" bed prevented orthostatic hypotension and the symptoms associated with it.

ORTHOSTATIC TACHYCARDIA

We have given the name orthostatic tachycardia to a syndrome which is characterized by an excessive acceleration of the heart when the patients change from the recumbent to the erect posture. Orthostatic exhaustion, blurring of vision, weakness on exercise and syncopal episodes may occur. There is usually no orthostatic hypotension present. Sweating is normal. This is a syndrome which seems identical with or similar to those characterized as effort syndrome, irritable heart or neurocirculatory asthenia. The symptoms and objective signs are immediately relieved when the patients lie down and as with orthostatic hypotension these patients exhibit an exacerbation of symptoms in the morning following a night of rest on a flat bed.

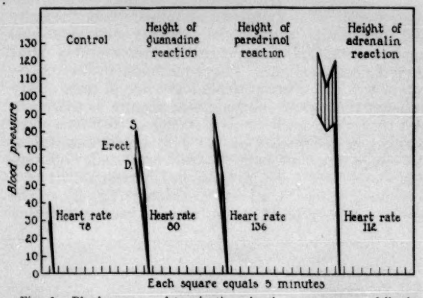

Fig. 3.—Blood pressure determinations in the erect posture following 0.75 Gm. of guanidine hydrochloride administered orally, 40 mg. of paredrinol sulfate administered intramuscularly and 1 mg. of epinephrine administered subcutaneously. In each instance the upper line indicates the systolic blood pressure and the lower line indicates the diastolic blood pressure. They are designated S and D respectively in that part of the chart showing the effect of guanidine. During the control period the patient fell in syncope at the end of one minute. At the height of the reactions to guanidine and paredrinol the patient fell at the end of five minutes. At the height of the reaction to epinephrine the patient fell at the end of ten minutes.

Symptoms and objective signs improve during the course of the day.

In our experience the Flack test has demonstrated an inherent defect in the mechanism for returning venous blood to the heart similar to that demonstrated in cases of orthostatic hypotension and it is our impression that the underlying pathogenesis is a diminution of "potential" of return of venous blood to the heart

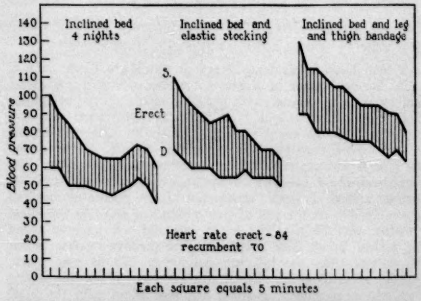

Fig. 4.—Blood pressure determinations in the erect posture after four nights of treatment with the tilted "head-up" bed. The patient was capable of standing for an hour without syncope.

rather than defective arterioles. It would appear that if these patients did not have orthostatic tachycardia they might have orthostatic hypotension. Following is an illustrative case of orthostatic tachycardia:

A physician aged 30 registered at the Mayo Clinic May 15, 1940. He complained of exhaustion and attacks of unconsciousness. Symptoms had begun a year and a half previous to registration, when he was working for long hours in a hospital spending many nights sitting up with his father, who was very

ill. At that time his wife noticed episodes characterized by unsteadiness in standing and walking, slowness and uncertainty of speech and pallor and exhaustion. His condition became progressively worse. The patient omitted breakfast once in September 1939 and an hour after arising fell and was unconscious for a minute. Hypoglycemia was suspected but studies of sugar in the blood did not confirm this suspicion. The exhaustion, weakness and difficulty in talking and walking became more pronounced, forcing the patient to terminate his hospital appointment and to go into general practice. In May 1940 he experienced two more episodes of unconsciousness of short duration.

A general physical examination demonstrated no abnormalities of note. A repetition of the dextrose tolerance studies and a thirty hour fast appeared to exclude hypoglycemia as a cause for the patient's ill health. Neurologic and electro-encephalographic examinations gave essentially negative results. The patient, however, had marked orthostatic tachycardia. In the recumbent position the blood pressure was 155/90, with a heart rate of 80 per minute. When in the erect posture the blood pressure varied between 120/80 and 100/70 and the heart rate averaged 150 beats per minute. The Flack test demonstrated a marked deficiency in the potential of venous return. When the patient blew the mercury column to the 40 mm. mark, the pulse disappeared at the end of ten seconds and the patient experienced a marked feeling of weakness and syncope.

In view of the obvious orthostatic vascular defects, the patient was questioned in detail concerning the time his symptoms occurred and it was discovered that the exhaustion, weakness and syncopal episodes had all occurred during the morning hours shortly after arising from a night of rest in bed. The patient and his wife had noticed that he improved as the day progressed unless he was subjected to some unusual strain.

The patient was placed on a tilted "head-up" bed, the head of which was raised 18 inches. On the following morning a distinct improvement occurred subjectively and this improvement was reflected in the heart rate with the patient standing. Following the second night on the tilted bed the patient's blood pressure in the erect position was 130/90, with a pulse rate of 80 beats per minute. This improvement continued as long as the patient was kept on the tilted bed at night. When he was again placed on a flat bed he reverted overnight to his previous condition, associated with a heart rate of 140 beats per minute when standing.

The patient returned home on a regimen of increased physical exercise and of sleeping on a tilted bed at night. His pulse rates in the erect posture and after mild exercise consistently remained less than 100 beats per minute. He experienced a return to normal health. One month after returning home, the patient was asked to sleep on a flat bed and within forty-eight hours his symptoms of exhaustion and weakness had returned and he experienced a severe syncopal episode with loss of consciousness. He promptly returned to the use of a tilted bed and all symptoms completely disappeared within twenty-four hours. He has written: "My work has been very heavy during the past weeks but I have been able to do it with far greater ease than ever before. After returning to the tilted bed there have been no periods of weakness or any other symptoms."

The following case is illustrative of a combination of orthostatic hypotension and tachycardia associated with the clinical picture of subacute combined sclerosis:

A woman aged 47, who registered at the Mayo Clinic June 10, 1940, complained of numbness and tingling of the finger tips, weakness and staggering gait of six months' duration. She had had anemia for twenty years and recurring attacks of glossitis for ten years. Achlorhydria was known to have been present for eight years. She had been treated with iron but not with liver.

The average number of erythrocytes was 3,300,000 per cubic millimeter of blood. The concentration of hemoglobin was 8.5 Gm. in each 100 cc. of blood and the color index was less than 1. Hypochromic anemia was apparent on microscopic examination. The majority of the erythrocytes were microcytes but there was an occasional macrocyte. There was no shift of the polymorphonuclear leukocytes to the right. Free hydrochloric acid was absent in the gastric contents, even after stimulation with histamine. Neurologic examination demonstrated the typical symptoms and signs of subacute combined sclerosis consisting of marked diminution of the deep reflexes of the lower extremities, bilateral Babinski phenomena, ataxic gait and absent vibration sense over the lower extremities and iliac crests. Joint sense of the legs was markedly impaired and Romberg's sign was present. During the process of the neurologic examination the patient fainted and examination of blood pressure in the recumbent and erect postures revealed the existence of orthostatic hypotension.

In the recumbent position the blood pressure averaged 160/110, a heart rate of 84. In the erect posture at the end of one minute of standing the blood pressure was 60/50, with a heart rate of 140. The patient was unable to stand for periods longer than three minutes without falling as a result of syncope. The Flack test gave markedly positive results. Detailed vascular examinations were conducted over a period of three days and very severe orthostatic tachycardia and hypotension of the degree already noted were found on every occasion. During this period of control the hematocrit estimation was 36 and studies of blood volume conducted by means of the congo red method demonstrated a total volume of 2,585 cc. of plasma or 45 cc. per kilogram of body weight. The total volume of whole blood was 4,038 cc. or 70 cc. per kilogram of body weight.

The patient was then placed on the tilted "head-up" bed with the head of the bed elevated 18 inches. The patient was encouraged to sit in a chair for as long as possible during the daytime and was forbidden to lie on a flat bed. During the course of three days no change could be detected in symptoms or in the signs of tachycardia or hypotension. On the fourth day, coincidental with the appearance of slight edema of the lower extremities, the clinical picture changed dramatically. In the recumbent position the blood pressure was 164/94, with a pulse rate of 80. With the patient in the erect posture, at the end of one minute the blood pressure was 166/98, with a heart rate of 96. At the end of ten minutes of continuous standing the blood pressure was 138/92, with a heart rate of 104. At the end of a half hour of continuous standing the blood pressure was 120/80, with a heart rate of 116. The patient was able to walk alone without assistance for the first time since admission to the hospital.

She was then placed on a flat bed for ten minutes, and studies of blood volume were conducted. The hematocrit index was 34. The total volume of plasma was 2,930 cc. or 51 cc. per kilogram of body weight. The total volume of whole blood was 4,448 cc. or 78 cc. per kilogram of body weight. There had been an apparent increase of 410 cc. in the volume of whole blood. Immediately after the determinations of blood volume were made, the patient was again placed on the tilted bed regimen. The improvement in symptoms, heart rate and blood pressure with the patient in the erect position was maintained.

In view of the fact that the patient had received three injections of liver parenterally at the time of her first admission to the hospital, the improvement could not be ascribed alone to the tilted bed. To evaluate the effect of the tilted bed the patient was placed on a flat bed for forty-eight hours. During the first twenty-four hours no appreciable change could be noted in the heart rate or blood pressure with the patient in the erect posture. At the end of forty-eight hours coinciding with the disappearance of the slight edema of the lower extremities the patient reverted to her previous condition. She was unable to stand for periods longer than a minute without syncope. The blood pressure with the patient recumbent was 140/80, with a heart rate of 80 beats per minute. Blood pressure in the erect posture at the end of half a minute was 60/45, with a heart rate of 130. The patient was again placed on the tilted "head-up" regimen and within forty-eight hours had completely regained postural vascular adaptability and was able to walk without assistance. During the course of three weeks of observation in the hospital she has remained on the tilted bed regimen and has not had a syncopal episode. The blood pressure and heart rate have remained consistently normal when she stands. With her increased ability to exercise, the edema of the lower extremities has disappeared. The signs of subacute combined sclerosis are still present. In spite of extensive liver parenterally administered the patient's blood picture has remained unchanged. The concentration of hemo-

globin is 8.1 Gm. per hundred cubic centimeters of blood. The erythrocytes number 4,100,000 per cubic millimeter of blood. Examination of the blood smear reveals hypochromic microcytic anemia with an occasional macrocyte.

An interesting feature of this case is the patient's history of twenty years of exhaustion and syncopal episodes. Every morning in these twenty years she had experienced severe exhaustion and dizziness during the first two hours after arising from bed. She had warned her class in school not to be concerned if they saw her put her head on her desk to keep from fainting. For twenty years she had not dared to kneel or stand in church for fear of fainting. During the afternoons and evenings of these twenty years the exhaustion would disappear and her tendency to faint would vanish, only to reappear again the following morning, after a night's rest in bed. Since institution of the tilted bed regimen the morning exhaustion, faintness and tendency toward syncope have disappeared in spite of the presence of subacute combined sclerosis. This patient was observed six months later. She had been treated persistently with liver extract and had slept on the "head-up" bed. The anemia and symptoms of subacute combined sclerosis were greatly improved. Orthostatic hypotension was absent but she stated that when she slept on a flat bed symptoms of this condition recurred.

COMMENT

It appears that there is an inherent defect in the ability to return venous blood to the heart when patients stand, in the syndromes of primary orthostatic hypotension and orthostatic tachycardia as well as in cases of secondary orthostatic hypotension following extensive sympathectomy for essential hypertension. This defect in the "potential" of venous return can be demonstrated objectively by means of the Flack test.

The tilted "head-up" bed has improved significantly the ability of the circulation of these patients who have orthostatic hypotension and orthostatic tachycardia to adapt itself to the erect posture as shown by objective study of the cardiac rates and blood pressures in the erect posture. These studies have corroborated the marked subjective improvement which follows this type of therapy. The improvement is maintained if use of the tilted bed at night is continued. Rest on the ordinary flat bed for a night or for several nights is sufficient to cause a reversal of the patient's condition and reestablish the original pattern of vascular maladaptation characterized by orthostatic tachycardia and hypotension and by recurrence of symptoms. Some patients with orthostatic tachycardia and orthostatic hypotension are not benefited by this type of treatment. The reasons are obscure.

It appears that rest and sleep on the tilted bed have prevented loss of that measure of postural adaptation which the patient himself has gained during the daytime, by some physiologic process attendant on increased activity in the erect posture. Whether this gain results from readjustments of activity of the autonomic nervous system to the muscles in the walls of the veins, whether there is a change in the tone of striated muscle, an increase in the content of extracellular fluid in the extremity, an increase in the volume of circulating blood or an intrinsic increase in venous or capillary tone is at the present time impossible to say. Investigation now being conducted suggests that the improvement in postural vascular adaptability coincides with an increase in the volume of circulating blood and a definite increase in the content of extracellular fluid in the lower extremities. It would seem logical to assume that the increased pressure of extracellular fluid would prevent in some degree pooling of blood in the legs with the patient in the upright position. We make the tentative suggestion that the content of extracellular fluid in the lower extremities is increased by the "head-up" posture and prevents pooling of venous blood in the legs as a result of increased tissue pressure. Return of venous blood to the heart is thus maintained in a fashion approaching normal. Studies are being conducted at the present time to determine the value of the "head-up" bed in cases of hypertensive headache, nocturnal epilepsy, exhaustion syndromes during convalescence and other disabilities that are associated with definite postural features.[7]

CONCLUSIONS

Elevation of the head of the bed for some patients with orthostatic tachycardia and for some patients with orthostatic hypotension prevents acceleration of the pulse rate and decrease in blood pressure when such patients stand. There is a coincidental improvement in symptoms. The "head-up" bed is in our experience the most satisfactory method of treatment for orthostatic tachycardia and orthostatic hypotension.

ABSTRACT OF DISCUSSION

DR. HORACE M. KORNS, Iowa City: The idea that the cause of orthostatic hypotension is to be sought in a disturbance of the mechanisms which normally provide, under all conditions, an adequate flow of blood from the veins to the heart is new, as far as I know, and is certainly attractive. Furthermore, it seems to me that likening the mechanism to that of nitrite shock is quite reasonable. Although, naturally, a larger series of cases will have to be collected before final conclusions can be drawn, the results obtained in these two cases by having the patient sleep with his head slightly elevated, which, theoretically, would tend to increase venous tone, strongly suggest that the authors' conception of the pathologic physiology of orthostatic hypotension is correct. I cannot help feeling, however, that hypotension alone is not the sole cause of the symptoms in this disease. After long observation of a typical case, Dr. W. L. Randall and I came to the conclusion that maintaining the blood pressure at an essentially normal level, which we were able to do by means of paredrine, was not enough in itself to relieve the patient of the lassitude and fatigability which are so characteristic. Only when, in addition, we produced psychic stimulation by giving amphetamine sulfate were the subjective manifestations dispelled. Patients with orthostatic hypotension may be subject to spontaneous hypoglycemia, as our patient was, and, if this complication is not recognized whenever it occurs, our efforts to evaluate any form of therapy may be confounded.

DR. O. P. J. FALK, St. Louis: The authors' significant observations are so definite and clearcut that they need little comment. This syndrome has had little light cast on it since the original observations of Bradbury and Eggleston in 1925. My interest in this syndrome was stimulated by observations on some sympathectomized hypertensive subjects on whom the usual phenomena of postural hypertension were observed. It seemed that there were a good many people who had not been sympathectomized but who had somewhat similar symptoms, and on checking postural blood pressure observations on them I was able to confirm the fact that there were a good many subclinical cases of postural hypotension going about unrecognized. I, like Drs. MacLean and Allen, have observed that these people respond to some of the drugs that they have mentioned, including amphetamine sulfate, neosynephrin and paredrine, but not to any permanent or sustained degree. Paredrine (20 mg. once or twice daily) seems to have the most marked and best sustained pressor effect. I wish to make a plea for a little more careful observation on some of these people who complain of such symptoms as undue fatigability and weakness or unsteadiness on standing, by checking their blood pressures in the stand-

7. Since this paper was written five additional patients with orthostatic hypotension and nineteen patients with orthostatic tachycardia have been treated on the "head-up" bed. Marked reversible improvement resulted in four of the cases of orthostatic hypotension and in sixteen of the cases of orthostatic tachycardia. Ten patients with chronic daily morning headaches have been studied. Six of these patients have obtained specific relief from pain in the head by the use of the "head-up" bed at night.

ing as well as the sitting and lying positions, so that these subclinical types will be recognized.

DR. A. R. MACLEAN, Rochester, Minn.: Several of our patients with orthostatic tachycardia have given histories suggestive of hypoglycemic episodes. Fasting blood sugar estimations, sugar tolerance curves and prolonged periods of fasting have definitely ruled out any primary hypoglycemic pathogenesis. However, blood sugar estimations in the lower range of normal values are not uncommon among individuals with tachycardia in the erect posture. This tendency may represent another phase in the disturbed physiology which results in a diminution of the venous return "potential." I wish to emphasize two important features of our work. We have very definite clinical proof that the "head-up" bed has accomplished a return of a large portion of postural vascular adaptability in patients with orthostatic hypotension and tachycardia. It has not cured them. We do not know how this improvement has been brought about. Some of our cases show an actual increase in the circulating blood volume following therapy. All of our cases appear to have an increase in the extracellular fluid content of the lower extremities. We can only say that the use of the head-up bed appears to have accomplished a relative increase in the circulating blood volume as compared to the total cross section of the vascular bed.

Clinical Notes, Suggestions and New Instruments

SUCCESSFUL SUBLINGUAL THERAPY IN ADDISON'S DISEASE

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Desoxycorticosterone acetate has been found highly effective in the treatment of Addison's disease. It is generally given in oil by subcutaneous or intramuscular injection but is being employed also in the form of pellets implanted under the skin. The latter method of administration is a precarious one, since there is no way of controlling dosage; excessive absorption of the active principle from pellets, as manifested by edema and anasarca, elevation of blood pressure to hypertensive heights and occasionally fatal circulatory collapse, has been reported by Loeb[1] and others. Subcutaneous and intramuscular injections, on the other hand, allow control of the dose administered, but they are often a source of great inconvenience and no little expense.

The ingestion of tablets of desoxycorticosterone acetate is for practical purposes valueless. Two of our patients with Addison's disease who ingested ten times the dose of desoxycorticosterone acetate effective by the subcutaneous route developed symptoms of adrenal cortical insufficiency. Kuizenga, Nelson and Cartland[2] have shown in experiments on the rat that this substance is less than one thirty-fifth as effective orally as parenterally.

In connection with this problem of an effective oral form of desoxycorticosterone acetate which would be rapidly absorbed, it was concluded that, since the ranine veins and ranine artery —besides the mass of capillaries and available lymphatics—are so near the surface and so exposed as to be more readily available for absorption of a substance when applied topically than any other part of the body, sublingual administration of steroids in solution appeared to be entirely practicable.

It was found that desoxycorticosterone acetate dissolved in propylene glycol administered by drops under the tongue was as effective in the cases herein reported as when given in oil subcutaneously or intramuscularly. Each cubic centimeter of propylene glycol contained 10 mg. of desoxycorticosterone acetate. The dropper used by the patients was such that 1 cc. of the solution was discharged as 40 drops. Hence 4 drops contained 1 mg. of desoxycorticosterone acetate. The dose was adjusted to the needs of the patient, from 8 to 24 drops of the solution, or 2 to 6 mg. of the active substance, being given daily in divided doses.

All six patients who have been receiving desoxycorticosterone acetate sublingually for from six to eight weeks are in excellent condition and are carrying on their usual occupations. A brief report of the status of these patients follows:

REPORT OF CASES

CASE 1.—H. E. L., a man aged 29, had had the characteristic signs and symptoms of Addison's disease since 1936. His usual weight of 135 pounds (61 Kg.) had fallen to 112 pounds (51 Kg.). A diffuse bronze pigmentation of the skin and of the buccal and pharyngeal mucous membranes was noted. Blood pressure ranged from 90 systolic, 40 diastolic to 100 systolic, 60 diastolic. Roentgenograms in 1936 failed to reveal any changes in the adrenals and lungs.

From April 1937 to September 1939 the patient was treated with various preparations of adrenal cortex extract. For about a year thereafter he received desoxycorticosterone acetate from 2.5 to 5 mg. intramuscularly once daily. By Aug. 22, 1940, his weight had increased to 123 pounds (56 Kg.), his blood pressure was 95 systolic, 60 diastolic and he felt well but, as during the past four years, he was unable to carry on his occupation. At that time sublingual administration of desoxycorticosterone acetate in propylene glycol was started, 4 drops being given five times a day (or 5 mg. of desoxycorticosterone acetate). He was instructed to take a well balanced diet and to discontinue the use of additional salt. When last seen, October 12, the patient weighed 127½ pounds (58 Kg.), his blood pressure was 95 systolic, 80 diastolic, and for the first time in four years he was carrying on his occupation as a ship inspector.

CASE 2.—M. L. M., a man aged 23, entered the hospital on June 18, 1940, his chief complaints being lassitude and extreme fatigability. Within a year his weight had fallen from 185 to 152 pounds (84 to 69 Kg.). A craving for salt had developed during the preceding three months. His blood pressure was 80 systolic, 60 diastolic and his skin showed deep pigmentation. Roentgenograms disclosed no abnormalities in the adrenal regions or the lungs.

Marked subjective improvement followed the administration of 10 mg. of desoxycorticosterone acetate once daily. His blood pressure had increased by July 16 to 110 systolic, 60 diastolic. Because of the development of edema at this time the dose of desoxycorticosterone acetate was decreased to 5 mg. a day. After the disappearance of edema the patient weighed 158 pounds (71.7 Kg.). Sublingual administration of desoxycorticosterone acetate in propylene glycol was started on August 27, the daily dose being 24 drops of the solution (containing 6 mg. of desoxycorticosterone acetate); at that time his blood pressure was 102 systolic, 60 diastolic and his weight 159½ pounds (72.3 Kg.). When the patient was last seen, October 10, he felt exceedingly well despite working long shifts as a taxicab driver. His weight was 165 pounds (75 Kg.) and his blood pressure 118 systolic, 80 diastolic.

CASE 3.—Baby R. M. (patient of Dr. H. E. Thelander), a boy born on Nov. 18, 1939, had symptoms of adrenal insufficiency dating from the time of his birth. The umbilical cord had been thrice encircled about the neck; cyanosis was marked and remained so for three days. On the eighth day after birth the baby vomited and had diarrhea. He responded well to the subcutaneous injection of salt solution and intravenous dextrose.

From the age of 5 weeks the baby received daily 1 mg. of desoxycorticosterone acetate by injection as well as adrenal cortex extract by mouth. His formula was made up with physiologic solution of sodium chloride. Temporary discon-

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The desoxycorticosterone acetate was supplied by the Schering Corporation for this study. The propylene glycol solution was made in our own laboratory. The crystalline material was added to the propylene glycol, which contained 10 per cent by volume of ethyl alcohol, and the material brought into solution by gentle warming. The alcohol was used to increase the solubility of the desoxycorticosterone acetate.

1. Loeb, R. F.: Adrenal Insufficiency, Bull. New York Acad. Med. **16**: 347-367 (June) 1940.

2. Kuizenga, M. H.; Nelson, J. W., and Cartland, G. F.: Comparative Parenteral and Oral Assays of Adrenal Cortical Hormone Substances, Am. J. Physiol. **130**: 298-303 (Aug.) 1940.

tinuance of the endocrine therapy was followed swiftly by signs of impending collapse. At the end of nine months the baby had gained well and reacted normally. On Aug. 25, 1940, sublingual use of desoxycorticosterone acetate in propylene glycol was begun, the dose being 2 drops five times a day (daily total of the substance, 2.5 mg.). After about seven weeks on sublingual therapy the baby is "strong and husky."

CASE 4.—D. J. W., a man aged 60, was admitted to the hospital on Aug. 19, 1940, in a state of collapse. He had had attacks of nausea and vomiting and pains in the abdomen for a period of two weeks. Considerable weight had been lost. His skin was deeply pigmented. The systolic blood pressure measured 90; the diastolic pressure could not be ascertained. Roentgenograms disclosed several rounded calcified foci in the lungs but no evidence of a change in the adrenals. The response to desoxycorticosterone acetate injected intramuscularly was highly satisfactory. At the time of discharge from the hospital, on September 5, the patient was receiving 5 mg. of desoxycorticosterone acetate daily.

When sublingual administration of desoxycorticosterone acetate in propylene glycol was begun on September 8 the patient felt well, his blood pressure was 115 systolic, 80 diastolic and his weight was 162 pounds (73.5 Kg.). The daily dose of the solution was 20 drops (or 5 mg. of the substance). On October 10 the patient stated that he felt very well and was fully able to carry on his occupation as a teacher. His blood pressure was 138 systolic, 80 diastolic and his weight 167 pounds (75.7 Kg.).

CASE 5.—S. K. (patient of Drs. Blair Holcomb, E. M. Burns and Hans Lisser), a man aged 35, since July 1937 had had attacks of nausea, vomiting and diarrhea which passed for "intestinal influenza." Following such an attack in 1938 the patient lost 30 pounds (13.6 Kg.) within a month. In July 1939, when seen by Drs. Holcomb and Burns, the patient presented a careworn and exhausted appearance, his skin was moderately pigmented, his blood pressure was 116 systolic, 80 diastolic, and he weighed 154 pounds (70 Kg.). He was given adrenal cortex extract subcutaneously and abundant salt by mouth. From Aug. 28 until Sept. 5, 1940, while under Dr. Lisser's care, the patient received desoxycorticosterone acetate intramuscularly 5 mg. a day and salt by mouth. He improved subjectively and his blood pressure rose to 140 systolic, 110 diastolic.

Since September 5 the patient has been taking desoxycorticosterone acetate in propylene glycol sublingually, 4 drops of the solution five times a day (a total daily dose of 5 mg. of the substance). On October 15 he weighed 152 pounds (69 Kg.), his blood pressure was 120 systolic, 86 diastolic, he appeared to be somewhat less pigmented and he stated that he felt better generally.

CASE 6.—Mrs. M. S. (patient of Dr. Helen Lee), aged 38, had had tuberculous peritonitis in 1927. In May 1938 she experienced a feeling of great fatigue and at about the same time noted that her skin was becoming pigmented. By April 1939 the tendency to fatigue had become more marked and there were occasional bouts of diarrhea. Roentgenograms disclosed a small calcified body overlying the upper pole of the left kidney. The blood pressure was 90 systolic, 50 diastolic and she weighed 131 pounds (59.4 Kg.). Impending collapse was prevented by the administration of adrenal cortex extract together with sodium chloride and sodium citrate. Since then she had taken adrenal cortex extract by mouth and by injection, together with large amounts of sodium chloride.

On Aug. 19, 1940, the sublingual use of desoxycorticosterone acetate in propylene glycol was begun. As in the other instances herein reported, the patient was instructed not to take salt in excess of that of the normal diet. At first 24 drops of the solution (6 mg. of the active substance) was given sublingually each day, but later, because of the development of edema about the ankles, the daily dose was reduced to 20 and later to 16 drops. The patient stated on October 19 that she felt considerably better on this regimen than she had heretofore and that she could now carry on her household and social activities without undue effort. On that day she weighed 140 pounds (63.5 Kg.) and had a blood pressure of 110 systolic, 80 diastolic.

SUMMARY

Desoxycorticosterone acetate dissolved in propylene glycol and administered by drops under the tongue has been found to be an effective form of replacement therapy in Addison's disease. The desoxycorticosterone acetate so administered seems to be as effective as that given in oil subcutaneously or intramuscularly.

Studies are now in progress as to the absorption of various endocrine substances when administered sublingually, particularly androgens and estrogens.

CHERRY STEM IN COMMON DUCT STONE

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LOS ANGELES

Foreign bodies are rarely considered a nucleus for stones found in the biliary tract. When encountered, however, they do present some interesting speculations.

REPORT OF CASE

A Negro youth aged 20, a student, admitted to the Los Angeles General Hospital Feb. 26, 1940, had been ill for ten days with nausea, vomiting and a sharp pain in the right upper quadrant of the abdomen. On the fifth day it was noted that he had acholic stools and also that he was jaundiced. He had a fever at times but no chills. There had been no antedating history of food intolerance or of similar attacks.

He was well developed and well nourished and in no great pain. The skin and scleras were jaundiced. There was rigidity in the right upper quadrant of the abdomen. Physical examination otherwise was negative. The hemoglobin content was 108 per cent, the erythrocyte count was 4,650,000 and the leukocyte count 13,400, with 83 per cent neutrophils, 3 per cent monocytes and 10 per cent lymphocytes. The urine gave a positive reaction for bile. The icteric index was 73. A flat x-ray plate of the abdomen was negative. His condition improved rapidly and he was discharged from the hospital March 7, only to return two days later with a recurrence of the same symptoms. He was again treated symptomatically and the condition rapidly cleared up again. March 21, a gallbladder dye study was made. There was no definite dye concentration: radiopaque calculi were not noted. He was discharged March 25. He felt well except for varying degrees of pain in the right upper quadrant and a poor appetite until May 22, when the pain again became severe and he reentered the hospital the following day.

His temperature was 103 F. and the blood pressure 105 systolic, 75 diastolic. He was in great pain, his face was flushed and the scleras were mildly icteric. There was rigidity of the right upper quadrant of the abdomen and the liver was palpable three fingerbreadths below the costal margin. The erythrocyte count was 4,500,000 and leukocyte count 13,100, with 86 per cent neutrophils. The icteric index was 40 on May 27 and 67 on May 30. He had an afternoon temperature of from 101 to 102 F. and stools were light yellow to gray until June 5, when he again became afebrile and asymptomatic.

At this time it was felt that an exploration should be done. Preoperative laboratory examination showed a cholesterol level of 208 mg. per hundred cubic centimeters of blood, a normal prothrombin content and an icteric index of 20, and oral cholecystography again showed no dye concentration.

July 1 a laparotomy was performed (by a preceding service). The gallbladder was reported as "only slightly thickened and almost normal in appearance" by the surgeon but found to contain very small flaky stones. The common duct was opened and some of the same material found. A catheter was placed in the common duct and the gallbladder removed. He made an uneventful recovery and on July 9 a cholangiogram revealed moderate dilatation of the intrahepatic ducts. There was a smooth 1.5 cm. ovoid shadow in the distal end of the common duct about which a small amount of dye could be forced. These conditions were consistent with an impacted stone at the distal end of the common bile duct. Several methods of flushing the

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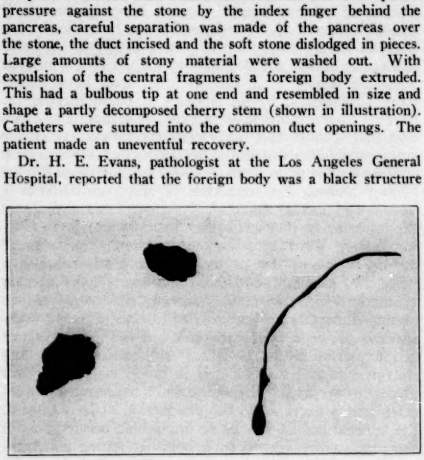
duct, after attempted fragmentation of the stone with ether, were attempted. Atropine, glyceryl trinitrate, desoxycholic acid and magnesium sulfate were of no avail, as the shadow persisted. The prothrombin time was checked and found normal.

July 29 exploration was done (by C. J. B.). The common duct was fixed in edematous adhesions from the previous operative procedure. It was explored but only flakes of stony material were obtained. The retroduodenal portion was then explored by mobilization of the duodenum according to the method of Kocher. The common duct was noted to traverse intrapancreatically and in that portion a fairly large stone could be readily palpated with the palm of the left hand behind the second portion of the duodenum. The stone was firmly lodged near the anterior surface of the pancreas and therefore was attacked through an anterior transpancreatic approach. With the palm of the left hand behind the duodenum and with upward pressure against the stone by the index finger behind the pancreas, careful separation was made of the pancreas over the stone, the duct incised and the soft stone dislodged in pieces. Large amounts of stony material were washed out. With expulsion of the central fragments a foreign body extruded. This had a bulbous tip at one end and resembled in size and shape a partly decomposed cherry stem (shown in illustration). Catheters were sutured into the common duct openings. The patient made an uneventful recovery.

Dr. H. E. Evans, pathologist at the Los Angeles General Hospital, reported that the foreign body was a black structure



Foreign body and some of the fragments of stone removed from the common duct (twice natural size.)

2.5 cm. long and 2 mm. in width and less than 1 mm. in thickness and had the appearance of some sort of vegetable or plant matter. A section was submitted to Dr. E. M. Hall, professor of pathology at the University of Southern California School of Medicine. His report stated that sections showed a number of small bits of moderately woody plant tissue and that many tracheal ducts were present with fairly thick walls.

The patient was a bright chap, a student of chemistry at the University of Southern California, and during his convalescence we asked him whether he had knowledge of ever eating cherries, stem and all. He replied that cherries had always been his favorite dish and that in earlier youth he had often eaten them by the double handful, at times not paying too much attention to stem or stone. We felt that we were safe in assuming that this was a cherry stem which had been ingested and by accident had slipped up the ampulla and had become lodged in the common duct, in time to become the nucleus for a stone.

COMMENT

Foreign bodies in the biliary tract are seldom encountered and are indeed a curiosity. A recent article by Toland [1] reviews the literature quite thoroughly. Among some of the foreign bodies removed from the common duct were swabs, rubber drains and nonabsorbable catgut ligatures, all from previous operations. As a nucleus for stones, pieces of suture were found most frequently, followed by an incidence each of bristle, thread and a piece of rubber drain. There are two reports of swallowing and migration: one a piece of wire and the other the handle of a spoon.

It is quite likely that if the centers of all single common duct stones were examined, particularly those occurring in apparently normal gallbladders without stones, the presence of a foreign body would be encountered at least occasionally.

523 West Sixth Street.

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Special Article

GLANDULAR PHYSIOLOGY AND THERAPY

THE ANTERIOR LOBE OF THE HYPOPHYSIS IN INTERMEDIARY METABOLISM

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This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.—ED.

The role of the anterior lobe of the pituitary in intermediary metabolism, especially in carbohydrate metabolism, has been reviewed by Houssay,[1] Russell,[2] Long,[3] Van Dyke,[4] Young,[5] Thomson and Collip [6] and others in recent years, in greater detail and with fuller bibliography than is possible in these pages. The subject is one of the greatest difficulty and complexity, since it is seldom possible to tell how widely the repercussions of any experimental interference may spread through the endocrine system. Great variations in behavior between species and between individuals in any one species are the rule rather than the exception. None of the anterior pituitary principles has yet been obtained in a state of indubitable purity, and any extract of the gland may or may not, depending on the source and the method of preparation, contain not only the thyrotropic and the corticotropic (adrenotropic) hormone (which must secondarily influence metabolic processes in many ways), the growth-promoting hormone (which presumably promotes anabolic processes even if its primary influence is on skeletal growth) and prolactin (which may directly or indirectly control metabolic adaptations to lactation) but also an uncertain number of principles active in metabolism but less clearly defined

1. Houssay, B. A.: Certain Relationships Between Parathyroids, Hypophysis and Pancreas, in Harvey Lectures, Baltimore, Williams & Wilkins Company, 1936, vol. 31, pp. 116-134; New England J. Med. **214**: 1128-1136 (June 4) 1936; Diabetes as a Disturbance of Endocrine Regulation, Am. J. M. Sc. **198**: 581-606 (May) 1937.

2. Russell, Jane A.: Relation of the Anterior Pituitary to Carbohydrate Metabolism, Physiol. Rev. **18**: 1-27 (Jan.) 1938.

3. Long, C. N. H.: Influence of Pituitary and Adrenal Glands on Diabetes Mellitus, in Harvey Lectures, Baltimore, Williams & Wilkins Company 1937, vol. 32, pp. 194-228; Medicine **16**: 215-247, (Sept.) 1937; Diabetes Mellitus in Light of Our Present Knowledge of Metabolism, Tr. & Stud., Coll. Physicians, Philadelphia **7**: 21-46 (April) 1939. Long, C. N. H., and White, A.: Intermediary Carbohydrate Metabolism, Ergebn. d. Physiol. **40**: 164-203, 1938.

4. Van Dyke, H. B.: Physiology and Pharmacology of the Pituitary Body, Chicago, University of Chicago Press, 1939, vol. 2.

5. Young, F. G.: Experimental Investigations on Relationship of Anterior Hypophysis to Diabetes Mellitus, Proc. Roy. Soc. Med. **31**: 1305-1316 (Sept.) 1938; Anterior Pituitary Gland and Diabetes Mellitus, New England J. Med. **221**: 635-646 (Oct. 26) 1939; Pituitary Gland and Carbohydrate Metabolism, Endocrinology **26**: 345-351 (Feb.) 1940.

6. Thomson, D. L., and Collip, J. B.: Endocrine Glands, Ann. Rev. Physiol. **2**: 309-346, 1940.

at present. For example, O'Donovan and Collip[7] demonstrated the existence of a factor which rapidly elevates the metabolic rate and depresses the respiratory quotient in normal and in thyroidectomized rabbits and guinea pigs and which is apparently derived from the pars intermedia, being closely associated with the melanophore-expanding hormone. Extracts which contain this factor may be largely freed from the "accepted" pituitary substances by exposure to high temperatures and still display manifold effects on intermediary metabolism. Even true posterior lobe principles (known and unknown) may be present in so-called anterior pituitary extracts, and may be overlooked.

A comparatively simple example of the apparent contradictions which abound in this field of study may be given. The hypophysectomized animal, with its atrophic thyroid, has a low metabolic rate, and its peripheral tissues consume abnormally small amounts of dextrose at all blood sugar levels[8]; in other words, its tolerance for injected dextrose is low,[9] but since the rate of absorption from the intestine is also greatly reduced, the tolerance for orally administered sugar is high.[10]

FASTING HYPOGLYCEMIA AND THE GLYCOSTATIC PHENOMENON

Many observers have noted that when hypophysectomized animals of any species are caused to fast, the blood sugar falls rapidly to levels dangerously low. In hypophysectomized monkeys, for example, after eighteen hours' fast the blood sugar averaged 59 mg. per hundred cubic centimeters, while in normal animals it was still 110 mg.;[11] and in rats, whose metabolism is more intense, the blood sugar concentration may be halved in eight hours' fasting after hypophysectomy, whereas controls show only a 20 per cent decrease.[12] Many hypophysectomized animals have died in hypoglycemia, and many have been dramatically resuscitated from a cold and deathlike torpor by injections of dextrose.[13] The phenomenon is not ascribable to a breakdown of the mechanism of glycogenolysis, since the stores of liver glycogen usually show similar rapid exhaustion. It has been claimed[14] that injected thyroxin will maintain the blood sugar of hypophysectomized animals during fasting, but it is more widely believed that the tendency to hypoglycemia is a consequence of the atrophy of the adrenal cortex which follows hypophysectomy, since adrenalectomized animals also show this tendency, especially if their mineral metabolism is controlled, and since injected cortical steroid substances will protect both hypophysectomized and adrenalectomized animals against it.[15]

Two rival interpretations of the hypoglycemic tendency have been put forward. On one hand, it is urged that the hypophysectomized (or adrenalectomized) animal prefers carbohydrate as a fuel and is spendthrift of its stores thereof. Evidence for this is seen in experiments in which dextrose is administered orally to rats which have fasted for twenty-four hours; the normal rat will oxidize about half the dextrose administered (in the following four hours) and will store about one third of it as liver and muscle glycogen in roughly equal shares, but the adrenalectomized or hypophysectomized rat will oxidize more and store less, whereas administration of adrenal cortex extract increases storage.[16] On the other hand, hypoglycemia may be an indication that the supply of new carbohydrate by glyconeogenesis is lagging behind the demands of the peripheral tissues. That the supply is, in fact, reduced after hypophysectomy is indicated by an analysis of blood leaving the liver;[17] furthermore, if one makes the orthodox assumption that a large and fairly constant proportion of the amino acids liberated in the breakdown of tissue protein constitutes the main source of new carbohydrate for the fasting animal, the excretion of nitrogen becomes a measure of the intensity of glyconeogenesis and shows the latter to be restricted after hypophysectomy. During fasting the nitrogen excretion tends to be low,[18] and is raised by the hormones of the adrenal cortex when they maintain the blood sugar level;[16] the increase in nitrogen excretion and in stored carbohydrate which occurs when rats are exposed to low atmospheric pressures is not seen after extirpation of the hypophysis or of the adrenal cortex.[19] There is, then, fair if not conclusive evidence that the fall in blood sugar and liver glycogen in fasting hypophysectomized animals indicates that a decrease in the production of hormones in the adrenal cortex has made impossible acceleration of the protein breakdown to a point at which glyconeogenesis would be adequate; and in any case the protective action of anterior pituitary extracts may be ascribed tentatively to the corticotropic factor which they contain.[20]

But the fasting hypophysectomized rat or mouse (other species have hardly been examined) shows a decrease in muscle glycogen which is more striking and appears more rapidly after extirpation of the gland than that in adrenalectomized animals; moreover, anterior pituitary extracts may display a "glycostatic" power to retard this decrease even when they contain little corticotropic substance and even in rats which have been adrenalectomized as well as hypophysecto-

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14. Soskin, Samuel; Levine, R., and Heller, R. E.: Role of Thyroid in Carbohydrate Disturbance Which Follows Hypophysectomy, Am. J. Physiol. **125**: 220-226 (Feb.) 1939.

15. Russell, Jane A., and Craig, J. M.: Adrenal Cortical Hormone and Anterior Pituitary Extract on Carbohydrate Levels in Fasted Hypophysectomized Rats, Proc. Soc. Exper. Biol. & Med. **39**: 59-62 (Oct.) 1938. Corey, E. L., and Britton, S. W.: Hypophysial and Adrenal Interrelationships and Carbohydrate Metabolism, Am. J. Physiol. **126**: 148-154 (May) 1939. Fitzgerald, O., and Verzar F.: Die Wirkung von Nebennierenrindenhormon auf den Glykogengehalt der Leber von hypophysektomierten Ratten, Arch. f. d. ges. Physiol. **242**: 30-34, 1939.

16. Long, C. N. H., and Katzin, B.: Effect of Adrenal Cortical Hormone on Carbohydrate Stores of Fasted Hypophysectomized Rats, Proc. Soc. Exper. Biol. & Med. **38**: 516-518 (May) 1938. Katzin, B., and Long, C. N. H.: Effect of Adrenal Cortical Extract on Carbohydrate and Protein Metabolism of the Rat, Am. J. Physiol. **126**: P551 (July) 1939.

17. Crandall, L. A., and Cherry, I. S.: Effects of Insulin and Glycine on Hepatic Glucose Output in Normal, Hypophysectomized, Adrenal-Denervated and Adrenalectomized Dogs, Am. J. Physiol. **125**: 658-673 (April) 1939.

18. Braier, B.: Metabolismo nitrogenado de los perros hipofisoprivos en el ayuno, Rev. Soc. argent. de biol. **7**: 140-157 (1931).

19. Evans, Gerald: Adrenal Cortex and Endogenous Carbohydrate Formation, Am. J. Physiol. **114**: 297-308 (Jan.) 1936.

20. Russell, Jane A.: Relationship of the Anterior Pituitary and Adrenal Cortex in Metabolism of Carbohydrate, Am. J. Physiol. **128**: 552-561 (Feb.) 1940.

mized.[21] During an eight hour fast the concentration of muscle glycogen may fall from 0.55 to 0.50 per cent in a normal rat and from 0.50 down to 0.30 per cent in a hypophysectomized rat; the higher respiratory quotient of the latter shows that the vanished carbohydrate has been oxidized, while the nitrogen excretion affords no evidence that glyconeogenesis diminished.[22] It is tempting to speculate that this using-up of muscle glycogen is due to a deficiency in the supply to the peripheral tissues not merely of dextrose, as in the adrenalectomized animal, but also of some other fuel (acetoacetic acid, for example; in which case this might be the inverse of the ketogenic phenomenon discussed later), but there is no supporting evidence at present for any such interpretation. It must be noted also, as a type of synergism yet unexplained, that the glycostatic phenomenon is most easily obtained when adrenal cortical principles are present in quantity, though it does not require that the gland itself should be intact.[20]

SENSITIVITY TO INSULIN AND THE GLYCOTROPIC PHENOMENON

The extreme sensitivity of the hypophysectomized animal to insulin, observed by Houssay and Magenta [23] in the dog, has been confirmed in many other species; it is from ten to thirty times greater than that of intact animals, the hypoglycemia being both intense and prolonged. Some increase in sensitivity is also observed in animals deprived of their adrenal medullae or of the sympathetic nervous system or even of the thyroid gland; but these observations seem irrelevant in face of the fact that pretreatment with suitable anterior pituitary extracts may decrease the exaggerated response to insulin of the hypophysectomized animal [24] and completely prevent insulin hypoglycemia in the normal animal; [25] this is called the "glycotropic" effect. In attempting an interpretation one must bear in mind that extracts showing glycotropic activity do not raise the blood sugar level or affect carbohydrate stores in normal animals, do not prevent the development of hypoglycemia in fasting hypophysectomized animals [26] and do not retard the fall in blood sugar that follows hepatectomy in the rabbit (though they prevent further acceleration of this fall by insulin [27]). Hence the factor is not a general inhibitor of carbohydrate consumption but a rather specific "anti-insulin"; yet any chemical interaction between these agents is unlikely, since the glycotropic factor must be administered some hours before the insulin to be effective. Part of the sugar which disappears from the blood under the influence of insulin is laid down in the muscles as glycogen, and it is possible that the glycotropic factor prevents this.[26] Beyond this the attempt at interpretation becomes frankly speculative; one could, for instance, work out a hypothesis equating the glycotropic and ketogenic effects, while, on the other hand, Jensen and Grattan [25d] produced evidence that the glycotropic and corticotropic factors are identical.

It was formerly thought that hypophysectomized animals were resistant to the hyperglycemic action of epinephrine and that this might explain their sensitivity to insulin, but it is only when the solution of epinephrine hydrochloride is injected subcutaneously that the sluggish circulation of the hypophysectomized animal, with its atrophic thyroid, prevents epinephrine from acting with its usual vigor.[28] Pretreatment with certain pituitary extracts diminishes the response to epinephrine; this is due to the presence of an unidentified factor probably originating in the posterior lobe.[29]

EFFECT OF HYPOPHYSECTOMY ON PANCREATIC DIABETES

No discovery has more sharply focused attention on the role of the anterior lobe of the hypophysis in carbohydrate metabolism than that of Houssay and Biasotti,[30] who showed, first in toads and then in dogs, that hypophysectomy profoundly modifies and moderates the intense diabetes usually produced by complete pancreatectomy; this discovery has been repeatedly confirmed and extended. Survival without insulin is greatly prolonged, and the animals are as likely to die in a hypoglycemic crisis as from diabetes; glycosuria and hyperglycemia do not become extreme, and are controlled by small amounts of insulin; ketosis is slight or absent; metabolic rate and nitrogen excretion do not show the usual increase, and weight is lost slowly if at all; liver glycogen stores are quite well maintained, and although the tolerance to administered dextrose is quite low,[31] excretion is not quantitative, and the respiratory quotient is not pegged at the fat level, while during fasting the low values of the urinary dextrose-nitrogen ratio indicate that much of the carbohydrate produced by glyconeogenesis is being consumed.

Long and Lukens [32a] showed in cats and dogs that adrenalectomy affected pancreatic diabetes in much the same way as hypophysectomy did in Houssay's experiments, and they proved that it was the cortex rather than the medulla of the adrenal which was of importance. Their animals received cortical extract in quantities sufficient to prevent serious disturbance of water and salt metabolism but apparently insufficient

21. Russell, Jane A., and Bennett, L. L.: Maintenance of Carbohydrate Levels in Fasted Hypophysectomized Rats Treated with Anterior Pituitary Extracts, Proc. Soc. Exper. Biol. & Med. **34:** 406-409 (May) 1936. Bennett, L. L.: Interrelation of Pituitary and Adrenal in the Control of Carbohydrate Levels in the Rat, Endocrinology **22:** 193-196 (Feb.) 1938.

22. Fisher, R. E.; Russell, Jane A., and Cori, C. F.: Glycogen Disappearance and Carbohydrate Oxidation in Hypophysectomized Rats, J. Biol. Chem. **115:** 627-634 (Oct.) 1936.

23. Houssay, B. A., and Magenta, M. A.: Sensibilidad en los perros hipofisoprivos a la insulina, Rev. Asoc. méd. argent. (Soc. de biol.) **37:** 389-406, 1924.

24. Houssay, B. A., and Potick, D.: Antagonisme entre l'hypophyse et l'insuline chez le crapaud, Compt. rend. Soc. de biol. **101:** 940-942 (July 17) 1929. di Benedetto, E.: Extrait antéro-hypophysaire et résistance à l'insuline, Compt. rend. Soc. de biol. **112:** 499-501 (Feb 10) 1933. Newton, W. H., and Young, F. G.: Influence of the Glycotropic (Anti-Insulin) Factor of the Anterior Hypophysis on the Insulin Sensitivity of the Hypophysectomized Rabbit, J. Physiol. **94:** 40-46 (Oct. 14) 1938.

25. (*a*) di Benedetto, E. C.: Extrait antéro-hypophysaire et résistance à l'insuline, Compt. rend. Soc. de biol. **112:** 499-501 (Feb. 10) 1933. (*b*) Cope, O., and Marks, H. P.: Further Experiments on Relation of Pituitary Gland to Action of Insulin and Adrenaline, J. Physiol. **83:** 157-176 (Dec. 31) 1934. (*c*) Young, F. G.: Identity and Mechanism of Action of the Glycotropic (Anti-Insulin) Substance of the Anterior Pituitary Gland, Biochem. J. **32:** 1521-1539 (Sept.) 1938. (*d*) Jensen, H., and Grattan, J. F.: Identity of the Glycotropic (Anti-Insulin) Substance of the Anterior Pituitary Gland, Am. J. Physiol. **128:** 270-275 (Jan.) 1940.

26. Russell, Jane A.: Action of Insulin and of Anterior Pituitary Extract in Normal and Hypophysectomized Rats, Am. J. Physiol. **124:** 774-790 (Dec.) 1938.

27. Himsworth, H. P., and Scott, D. B. McN.: Action of Young's Glycotropic Factor of Anterior Pituitary Gland, J. Physiol. **92:** 183-207 (March 14) 1938.

28. Braier, B.: Influence de l'adrénaline sur le métabolisme azoté et la glycémie des chiens hypophysoprives, Compt. rend. Soc. de biol. **108:** 491-493 (Oct. 30) 1931. Heinbecker, P. T., and Weichselbaum, T. E.: Blood Sugar Response to Intraperitoneal Epinephrine Injections in Normal and Hypophysectomized Dogs, Proc. Soc. Exper. Biol. & Med. **37:** 527-529 (Dec.) 1937. Russell and Cori.[9]

29. Stenström, T.: Das Pituitrin und die Adrenalinhyperglykämie, Biochem. Ztschr. **58:** 472-482, 1914. Neufeld, A. H., and Collip, J. B.: Further Studies on the Antagonist to Adrenalin Hyperglycemia in Pituitary Extracts, Endocrinology **25:** 775-781 (Nov.) 1939.

30. Houssay, B. A., and Biasotti, A.: Hypophysectomie et diabète pancréatique chez le crapaud, Compt. rend. Soc. de biol. **104:** 407-410 (May 30) 1930; Le diabète pancréatique des chiens hypophysectomisés, ibid. **105:** 121-123 (Oct. 16) 1930.

31. Chambers, W. H.; Sweet, J. E., and Chandler, J. P.: Carbohydrate Metabolism in the Hypophysectomized Depancreatized Dog, Am. J. Physiol. **119:** 286-287 (June) 1937. Lichtman, A. L.: Fatty Acids and Glucose in Blood of Depancreatized Dogs, J. Biol. Chem. **120:** 35-40 (Aug.) 1937.

32. (*a*) Long, C. N. H., and Lukens, F. D. W.: The Effects of Adrenalectomy and Hypophysectomy upon Experimental Diabetes in the Cat, J. Exper. Med. **63:** 465-490 (April) 1936. (*b*) Long, C. N. H.; Lukens, F. D. W., and Dohan, F. C.: Adrenalectomized-Depancreatized Dogs, Proc. Soc. Exper. Biol. & Med. **36:** 553-554 (May) 1937.

to replace the function of the glands in carbohydrate metabolism; in later experiments they found that adrenalectomy abolished glycosuria in partially depancreatized rats, maintained after the second operation with saline solution.[3] The effect of thyroidectomy on pancreatic diabetes is slight and inconstant.

Discussion of these adrenal-pituitary relations will be deferred until the action of pituitary extracts on animals doubly operated on has been described, but it may be well to point out here that while in the dog and still more in the cat pancreatectomy alone produces exceedingly severe and rapidly fatal diabetes, there are other species (including pig, sheep and monkey) in which the diabetes is of a relatively mild type, with low dextrose-nitrogen ratios, little ketosis and great sensitivity to insulin—resembling the condition observed in the hypophysectomized-depancreatized, or "Houssay," dog or cat, or clinical diabetes of moderate severity. It is especially interesting to note that cases have been encountered in the clinic in which fibrotic or other change had almost completely obliterated the islet tissue of the pancreas, yet the diabetes resembled that produced by pancreatectomy in the monkey [33] rather than that in the dog, and was less severe than in many other cases of clinical diabetes in which there was little or no pathologic alteration of the islets.

DIABETOGENIC ACTION OF ANTERIOR PITUITARY EXTRACTS

The injection of anterior pituitary extracts of many kinds is not infrequently followed by slight transient hyperglycemia; this has been ascribed to contamination with posterior-pituitary principles or to nonspecific stimulation of epinephrine discharge, and does not in any way merit the name "diabetogenic." But if fresh simple extracts that have been cautiously prepared are administered in large doses day after day to well nourished dogs, cats or rabbits, one may observe in many individual animals after some days a gradual but maintained rise of the blood sugar beyond glycosuric levels, moderate ketonuria, increased excretion of nitrogen and other symptoms of diabetes.[34] At its height the condition may simulate in severity that produced by pancreatectomy, from which it differs chiefly in maintenance of body weight, maintenance of liver glycogen and resistance to insulin treatment.[5] It is interesting to compare this with the resistance to insulin exhibited in those patients with diabetes in whom acromegaly and hyperthyroidism point to hyperfunction of the anterior lobe of the pituitary as the primary disturbance. Yet it must not be supposed that the secretion of insulin continues unimpaired during the temporary diabetes produced by anterior pituitary extracts, for degranulation and hydropic degeneration of the beta cells of the islets of Langerhans occur,[35] the amount of insulin extractable from the pancreas falls to a low level,[36] and when such a pancreas is transplanted into a diabetic animal it seems to produce little insulin.[37] It seems unlikely that the anterior pituitary extract should have a directly harmful influence on the pancreas and more probable that the islets become exhausted because of the tendency of substances in the pituitary extract to elevate blood sugar and neutralize insulin action; similar changes in the islets are observed when blood sugar levels are kept high by injections of dextrose,[38] and a supply of extra insulin may protect the islets against the anterior pituitary extract.[39]

Extracts which are diabetogenic in the dog have no such action in the guinea pig, mouse or rat; in the last, indeed, they cause a considerable increase in the quantity of islet tissue found in the pancreas and in the amount of insulin extractable therefrom; [40] this "pancreotropic" effect is not now obtainable in the circumstances in which it was first described.[41] One concludes that in some species the islet tissue is sufficiently adaptable to bear any strain that has yet been thrown upon it.

The type of experimental diabetes described in the foregoing paragraphs is well called temporary. Not merely does it soon subside after the treatment has ceased, but it does not persist for more than a few days even when the injections are continued at a constant level; the diabetic symptoms vanish, though resistance to insulin (glycotropic effect) persists. But an increase in the amount of anterior pituitary extract given will reestablish the diabetic state for a few days more, until finally a dose is reached (say, the equivalent of 25 Gm. of fresh gland daily) at which the animal can no longer escape: the diabetes not only persists as long as treatment continues but reaches a point (often marked by transient exacerbation of ketonuria) at which the degeneration of the islets becomes irreversible, so that the diabetes continues indefinitely and unabated even when the extract is withdrawn.[42]

Such permanently diabetic dogs vary in the intensity of diabetes exhibited, but in general their insulin requirements, sugar excretion and dextrose-nitrogen ratios are even higher than those usually recorded for depancreatized dogs on the same diet; ketonuria, however, may be low in the early stages, weight is better maintained, and survival without insulin is much longer; [43] the islet tissue is altered to a variable extent,

33. Collip, J. B.; Selye, Hans, and Neufeld, A. H.: Experimental Pancreatic Diabetes in the Monkey, Am. J. Physiol. **119:** 332 (June) 1937; Canad. M. A. J. **37:** 287-288 (Sept.) 1937.

34. Johns, W. S.; O'Mulvenny, T. O.; Potts, E. B., and Laughton, N. B.: Studies on the Anterior Lobe of the Pituitary Body, Am. J. Physiol. **80:** 100-106 (March) 1927. Evans, H. M.; Meyer, Karl; Simpson, Miriam E., and Reichert, F. L.: Disturbance of Carbohydrate Metabolism of Normal Dogs Injected with the Hypophysial Growth Hormone, Proc. Soc. Exper. Biol. & Med. **29:** 857-858 (April) 1932. Baumann, E. J., and Marine, David: Glycosuria in Rabbits Following Injections of Saline Extract of Anterior Pituitary, ibid. **29:** 1220-1223, (June) 1932. Houssay, B. A.; Biasotti, A., and Rietti, C. T.: Acción diabetogena del extracto antero-hipofisario, Rev. Soc. argent. de biol. **8:** 469-481 (Aug.-Sept.) 1932. Evans, E. I.: Diabetogenic Principle of Anterior Pituitary, Proc. Soc. Exper. Biol. & Med. **30:** 1370-1371 (June) 1933.

35. Richardson, K. C., and Young, F. G.: Histology of Diabetes Induced in Dogs by Injection of Anterior-Pituitary Extracts, Lancet **1:** 1098-1101 (May 14) 1938. Richardson, K. C.: Influence of Diabetogenic Anterior Pituitary Extracts on the Islets of Langerhans in Dogs, Proc. Roy. Soc., London, s. B **128:** 153-169 (Jan. 4) 1940.

36. Best, C. H.; Campbell, James, and Haist, R. E.: Effect of Anterior Pituitary Extracts on the Insulin Content of the Pancreas, J. Physiol. **97:** 200-206 (Dec. 14) 1939.

37. Houssay, B. A., and Foglia, V. G.: Diabetes antero-hipofisaria y funcion endocrina pancreatica, Rev. Soc. argent. de biol. **12:** 237-252 (Aug.) 1936.

38. Woerner, C. A.: Studies of Islets of Langerhans After Continuous Intravenous Injection of Dextrose, Anat. Rec. **71:** 33-57 (May 25) 1938.

39. Campbell, James; Haist, R. E.; Ham, A. W., and Best, C. H.: Insulin Content of the Pancreas as Influenced by Anterior Pituitary Extract and Insulin, Am. J. Physiol. **129:** P328-P329 (May) 1940.

40. Richardson, K. C., and Young, F. G.: Pancreotropic Action of Anterior Pituitary Extracts, J. Physiol. **91:** 352-364 (Dec. 14) 1937. Marks, H. P., and Young, F. G.: Pancreotropic Action of Anterior Pituitary Extracts, Chem. & Industry **58:** 652, 1939.

41. Anselmino, K. J.; Herold, L., and Hoffmann, F.: Ueber die pankreatrope Wirkung von Hypophysenvorderlappenextrakten, Klin. Wchnschr. **12:** 1245-1247 (Aug. 12) 1933.

42. Young, F. G.: Permanent Experimental Diabetes Produced by Pituitary (Anterior Lobe) Injections, Lancet **2:** 372-374 (Aug. 14) 1937; Preparation and Properties of Diabetogenic Extracts, J. Endocrinol. **1:** 339-355 (Nov.) 1939. Campbell, James and Best, C. H.: Production of Diabetes in Dogs by Anterior-Pituitary Extracts, Lancet **1:** 1444-1445 (June) 1938. Houssay, B. A., and Biasotti, A.: Acción diabetogena de diversas hormonas hipofisarias, Rev. Soc. argent. de biol. **14:** 297-307 (Aug.) 1938. Dohan, F. C., and Lukens, F. D. W.: Persistent Diabetes Following Injection of Anterior Pituitary Extract, Am. J. Physiol. **125:** 188-195 (Jan.) 1939. Loubatières, A.: Récherches sur le diabète sucré permanent consécutif aux injections d'extrait de lobe antérieur d'hypophyse chez le chien normal, Compt. rend. Acad. d. sc. **208:** 1933-1935 (June 12) 1939.

43. Marks, H. P., and Young, F. G.: Observations on the Metabolism of Dogs Made Permanently Diabetic by Treatment with Anterior Pituitary Extract, J. Endocrinol. **1:** 470-510 (Dec.) 1939.

and hardly any insulin can be extracted from it; surgical removal of the pancreas may have little influence, once the permanent diabetes is established. One feels that if there are real differences between dogs that are diabetic because their islet tissue collapsed under treatment with an anterior pituitary extract weeks or months previously and dogs that are diabetic because the whole pancreas has been removed, such differences must be due to the loss of the pancreatic acinar tissue in the latter rather than to persistence of any extrapancreatic effect of the anterior pituitary extract in the former.

ANTERIOR PITUITARY EXTRACTS IN DEPANCREATIZED ANIMALS

It is probably desirable to restrict the term "diabetogenic" to extracts capable of producing temporary if not permanent diabetes in normal dogs,[5] but it has sometimes been applied in a rather different way. To produce diabetes in normal animals, even in the susceptible individuals of relatively susceptible species, one requires large doses of extracts which have been carefully protected from the destructive action of heat or powerful reagents; but in subtotally depancreatized animals (even of resistant species such as the rat) or hypophysectomized-depancreatized ("Houssay") animals, diabetic symptoms can be elicited easily, or intensified if already present, with moderate doses of extracts of many kinds. The conclusion is inescapable that true diabetogenic potency involves the action of one or more very labile factors as well as of relatively stable factors that may be effective by themselves in animals deprived of all or most of their insulin-producing tissue.

Among these relatively stable factors one may certainly include the corticotropic principle, for extracts which evoke intense glycosuria and ketonuria in hypophysectomized-depancreatized cats have little or no effect on adrenalectomized-depancreatized animals;[42a] adrenal cortex extract causes glycosuria in subtotally depancreatized (but not in normal) rats.[44] But in the latter test the action of the cortical steroids is not as great when they are administered by themselves as when they are administered simultaneously with anterior pituitary extracts (a further example of the type of synergism already discussed[20]); moreover, anterior pituitary extracts may evoke glycosuria in partially depancreatized adrenalectomized dogs;[45] hence the corticotropic factor is certainly not the only one involved. In considering the identity of the labile factor or factors, one naturally thinks of the "growth hormone," which is closely associated with diabetogenic activity;[46] and it has been shown recently that even brief heat treatment largely destroys the striking power of fresh anterior pituitary extracts to increase the body glycogen of normal fasting mice.[47] In viewing the diabetogenic phenomenon as a whole one may cite the evidence (quoted in the discussion of the hypoglycemia of fasting animals) that anterior pituitary principles often tend to increase glyconeogenesis; one may be inclined also to credit them with the power to diminish the utilization of carbohydrate by the peripheral tissues, even if this seems to elude direct demonstration,[14] and one has, unfortunately, several different unsupported interpretations of the glycotropic phenomenon to draw on as required.

THE KETOGENIC PHENOMENON

The urinary excretion of acetone bodies by the fasting or fat-fed rat, normally quite small, may be greatly increased by injecting anterior pituitary extracts;[48] there is a simultaneous rise in blood ketones, which is a more sensitive and dependable index of the phenomenon, since acetoacetic and hydroxybutyric acids are to some extent threshold substances. Parallel observations have been made in other species, including the mouse, guinea pig, rabbit, dog and man. The effect is lessened but not abolished after adrenalectomy.

A general discussion of this phenomenon has been published elsewhere;[49] there is good evidence that it indicates an increased outpouring of ketone bodies by the liver rather than a diminished utilization of them;[50] and in general the ketosis is accompanied by a transfer of fat from the depots to the liver, in which large quantities may accumulate.[51] There is accordingly a good deal of support for the view that the phenomenon represents a general stimulation of fat catabolism beyond the capacity of the body to oxidize the ketonic final products. Yet other possibilities exist; fatty acids are not the only conceivable source of acetone bodies, and there may well be different types of ketonemia; if stimulation of fat metabolism does occur, it may be secondary rather than direct.

Shipley and Long,[46] for instance, have suggested that the primary effect of crude extracts of the anterior lobe may be to *retard* the breakdown of tissue protein so that the energy requirements of the body are met by drawing on preformed carbohydrate stores (which are rapidly exhausted to the point of hypoglycemia[52]) and on the fat depots, whose overactive response may produce ketonemia. Some retardation of protein catabolism is, as already pointed out, required of a "growth hormone," and it has in fact been observed in many experiments.[53] At first sight this appears to be a bewildering contradiction of the thesis already developed, that anterior

44. Fry, E. G.; Long, C. N. H., and Ritter, H. B.: Aggravation of Pancreatic Diabetes by Adrenal Cortical Extract, Am. J. Physiol. **126:** 497 (July) 1939.

45. Houssay, B. A., and Biasotti, A.: Acción diabetogena anterohipofisaria en perros sin suprarenales, Rev. Soc. argent. de biol. **14:** 308-314 (Aug.) 1938.

46. Shipley, R. A., and Long C. N. H.: Studies on the Ketogenic Activity of the Anterior Pituitary, Biochem. J. **32:** 2242-2256 (Dec.) 1938.

47. Neufeld, A. H.; Scoggan, S. M., and Stewart, G. S.: Effect of Pituitary Preparations on the Total Body Glycogen, Water, Nitrogen, and Fat of Fasted Mice, Endocrinology **27:** 132-136 (July) 1940.

48. Burn, J. H., and Ling, H. W.: Ketonuria in Rats on a Fat Diet After Injection of Pituitary (Anterior Lobe) Extract, J. Physiol. **69:** xix (March 15) 1930; Excretion of Acetone Bodies on a Fat Diet as Affected by the Injection of Pituitary (Anterior Lobe) Extract and by Pregnancy, Quart. J. Pharm. & Pharmacol **6:** 31-38 (Oct.-Dec.) 1933. Hoffmann, F., and Anselmino, K. J.: Das Fettstoffwechselhormon des Hypophysenvorderlappens, Klin. Wchnschr. **10:** 2383-2386 (Dec. 26) 1931. Magistris, L.: Das Fettstoffwechselhormon des Hypophysenvorderlappens, Endokrinologie **11:** 176-191, 1932. Butts, J. S.; Cutler, C. H., and Deuel, H. J.: Sexual Variation in Carbohydrate Metabolism: Role of Anterior Pituitary in Metabolism of Diacetic Acid, J. Biol. Chem. **105:** 45-58 (April) 1934. Black, P. T.; Collip, J. B., and Thomson, D. L.: Effect of Anterior Pituitary Extracts on Acetone Body Excretion in the Rat, J. Physiol. **82:** 385-391 (Oct. 17) 1934. Shipley, R. A.: Effect of Adrenalectomy on Ketosis Produced in Rats by Anterior Pituitary Extract, Endocrinology **26:** 900-905 (May) 1940.

49. Thomson, D. L.: Anterior Pituitary and Metabolism of Acetone Bodies, A. Research Nerv. & Ment. Dis., Proc. (1936) **17:** 257-267, 1938.

50. Mirsky, I. A.: Source of Blood Acetone Resulting from Administration of Ketogenic Principle of Anterior Hypophysis, Am. J. Physiol. **115:** 424-428 (April) 1936.

51. Best, C. H., and Campbell, James: Anterior Pituitary Extracts and Liver Fat, J. Physiol. **86:** 190-203 (Feb. 8) 1936; Effect of Anterior Pituitary Extract on Liver Fat of Various Animals, ibid. **92:** 91-110 (Feb. 16) 1938. Barrett, H. M.; Best, C. H., and Ridout, J. H.: Study of Source of Liver Fat Using Deuterium as Indicator, ibid. **92:** 367-381 (Sept. 16) 1938. Neufeld, A. H., and Collip, J. B.: Effect of Pituitary Extracts on Ketonuria, Fat Content and Fat Distribution in the Liver and Tissues of Mice, Endocrinology **25:** 768-774 (Nov.) 1939.

52. Harrison, H. C., and Long, C. N. H.: Effect of Anterior Pituitary Extract on the Metabolism of Fasting Normal and Adrenalectomized Rats, Am. J. Physiol. **126:** 526-527 (July) 1938.

53. Teel, H. M., and Cushing, Harvey: Studies in the Physiological Properties of Growth-Promoting Extracts of the Anterior Hypophysis, Endocrinology **14:** 157-163 (May-June) 1930. Gaebler, O. H.: Some Effects of Anterior Pituitary Extracts on Nitrogen Metabolism, Water Balance, and Energy Metabolism, J. Exper. med. **57:** 349-363 (March) 1933. Lee, M. O., and Schaffer, N. K.: Anterior Pituitary Growth Hormone and the Composition of Growth, J. Nutrition **7:** 337-363 (March 10) 1934. Schaffer, N. K., and Lee, M. O.: Effect of Anterior Pituitary Growth Hormone on Protein Metabolism, J. Biol. Chem. **108:** 355-371 (Feb.) 1935.

pituitary extracts (especially those containing the corticotropic principle) stimulate protein breakdown and glyconeogenesis, and certainly it is probable that one is here dealing with another factor. It is quite possible that the balance is held by the islets of Langerhans; nitrogen retention will be favored as long as they continue to produce sufficient insulin, nitrogen loss when they break down under the stimulus. Thus Mirsky,[54] using the rate of increase of nonprotein nitrogen in the blood of nephrectomized dogs to measure the catabolism of protein, finds it to be increased by crude extracts of the anterior lobe in depancreatized (diabetic) animals but slightly decreased in normal ones.

A great deal of effort has been expended in the study of the chemical and physical properties of the factors described and in attempts to separate them by chemical means; the results are of great importance to those actually working in the field but are unfortunately so full of apparent contradictions that they can rarely be used to support general statements and have accordingly been given little attention in this review.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING CHAPTER, WHICH IS THE THIRD OF A SERIES ON AMPUTATIONS AND ARTIFICIAL LIMBS TO APPEAR IN THIS COLUMN. WHEN COMPLETED, THE SERIES WILL BE PUBLISHED IN THE FORM OF A HANDBOOK ON AMPUTATIONS. THE COUNCIL WISHES TO EXPRESS ITS APPRECIATION FOR THE COOPERATION OF ITS GROUP OF CONSULTANTS ON ARTIFICIAL LIMBS. THE COUNCIL IS REPRESENTED BY DRS. FRANK D. DICKSON, HARRY E. MOCK, FRANK R. OBER, S. PERRY ROGERS, PAUL STEELE AND PHILIP WILSON, AND THE ASSOCIATION OF LIMB MANUFACTURERS OF AMERICA IS REPRESENTED BY MESSRS. MCCARTHY HANGER SR., W. E. ISLE, JOSEPH A. SPIEVAK, DAVID E. STOLPE AND J. B. KORRADY.

HOWARD A. CARTER, Secretary.

CHAPTER III. SITES OF ELECTION FOR AMPUTATION

Certain "sites of election" are generally recognized as promising functional amputation stumps, and numerous methods of operation at different sites have been planned with the same objective of function. These sites may be considered in order from below upward.

1. LOWER EXTREMITY

Amputation of toes results only in the slight loss of spring to the gait provided by the final push-off of the toes in each step. The natural weight bearing areas of heel and metatarsal heads are undisturbed, muscular control of the foot is not seriously interfered with, and satisfactory leverage remains. No prosthesis is required.

Amputation through the metatarsals sacrifices the normal weight bearing surfaces beneath the heads of these bones. A plantar flap compensates somewhat by retaining soft tissue integuments physiologically adapted to weight bearing. Muscular control of the ankle is sacrificed no more than in amputation of the toes, although cutting through the short plantar muscles impairs further the support of the arch. Leverage is lost in proportion as the site of amputation progresses backward, and function decreases accordingly. Lisfranc's amputation through the tarsometatarsal joints is as far back as one can go without this loss of leverage becoming prohibitive. It must be remembered that these amputations are usually due to trauma and that the injured tissues seldom allow amputation at this level.

54. Mirsky, I. A.: The Influence of the Anterior Pituitary Gland on Protein Metabolism, Endocrinology **25**: 52-56 (July) 1939.

Amputations between the tarsometatarsal and the ankle joints are condemned. Chopart's amputation, leaving only the astragalus and the calcaneus, is the one most commonly employed. Two factors, loss of the natural attachments of the anterior tibial, peroneal and toe extensor muscles and further shortening of the lever of the foot, render equinus deformity of the stump almost inevitable. The appliance for such amputations is as unwieldy and unsightly as that for an amputation just above the ankle, and the resultant function is not so good.

Amputations immediately above the ankle joint are called Syme's or Pirogoff's. In both operations the tibia and fibula are sawed horizontally within 1 inch of the ankle joint. Both employ a posterior flap composed of all the layers of soft tissue from the tip of the heel, and both leave a transverse anterior scar. In Pirogoff's technic the posterior part of the os calcis, sawed vertically, is left in the flap and is opposed to the cut surface of the tibia. Both amputations require careful surgical technic in care of the vessels and nerves and in snug tailoring of the flaps. Neither is likely to succeed in the presence of infection.

Amputations at this level were in high favor a century ago. The patient could frequently walk, or even run, without any appliance. The prosthesis is bulky. It must be entered from the front and laced snugly above the bulbous tip of the stump. It is more serviceable without any ankle joint mechanism. Modern limb manufacturers hold in disfavor any amputation between the heads of the metatarsals and the middle of the leg because of the unsightly appearance of the prosthesis. A recent English compilation of late results in Syme amputations performed during the war of 1914-1918 shows that almost all of these stumps have now been reamputated because of circulatory complications.

The optimum site for amputation in the shaft of the leg is its middle third. In the adult this will vary between 5 and 7 inches from the joint line, depending on the height of the patient and the length of the limb. Longer stumps are apt to be insufficiently covered, to be tender and to suffer vascular difficulties. Longer stumps also require an unsightly bulkiness in the shank of the prosthesis. The shorter stumps, cut through cancellous bone, are likely to permit a larger degree of end bearing, although most of them require that the greater part of the weight be borne on the sloping surfaces of the head of the tibia. The minimum length of tibia for satisfactory leverage is 2½ inches. The fibula should usually be retained for its function in controlling rotation of the prosthesis. In very short stumps it may be removed entirely. If retained it should be cut from 1 to 2 inches shorter than the tibia, depending on the length of the stump. In children the fibula should be cut three inches shorter or else its epiphysis should be arrested. If the fibula is removed, care should be exercised to remove all its periosteum as well.

Amputation through the leg is conveniently performed with the patient prone (face downward). The bones should be denuded of periosteum for a distance of 1 inch and all sharp corners removed, the anterior border of the fibia with a saw and all sharp edges with a rasp. The bones should be covered with a posterior flap composed of the tendinous aponeurosis of the gastrocnemius and fascia with little or no muscle, and in turn by an anterior skin flap long enough to leave a posterior scar. Redundance of flaps must be avoided. Postoperative splinting is especially important to prevent contracture of the knee. Massage, active exercise

and hardening of the stump are recommended. Early walking on a temporary prosthesis is advantageous.

Amputation by disarticulation at the knee joint, popular a century ago, has fallen into such disuse that it is now generally employed only as a temporary emergency procedure. Objections based on mechanical reasons, such as bulkiness and unsightliness of the prosthesis, and the necessity of disproportionate length of thigh and leg, are unfounded under modern facilities of artificial limb manufacture. Some disarticulation stumps have been unsatisfactory from the functional standpoint for one of two reasons: The patella floating free on the front of the thigh may remain so tender as to prohibit encasement in a socket. Other stumps have permitted painless end bearing at first only to undergo atrophy and ulceration of the terminal integuments after months or years of function.

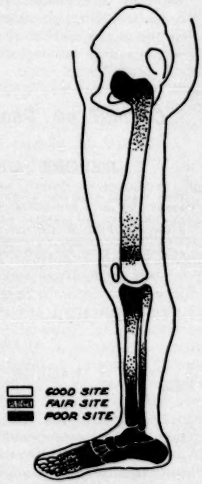
Theoretically, numerous physiologic and mechanical advantages are apparent at this level. The femoral condyles and the patella, as well as all the soft tissues in an anterior flap, are physiologically adapted to withstanding pressure. Ligation of the popliteal artery below its superior genicular branches leaves a rich anastomosis of vessels at the end of the stump. Retention of the lower femoral epiphysis assures normal growth of the stump in a child. Recent modifications in operative technic, described by Rogers, are directed against the previous faults in these stumps. Arthrodesis of the patella to the front of the femur in its anatomic position eliminates any tenderness and increases the end bearing surface area. Fixation of all the hamstring tendons to the tip of the patellar tendon in the posterior intercondylar notch relieves the terminal soft tissues of tension and subjects them only to pressure, which they are adapted to bear. A limited experience with this technic promises relief from the late complications previously encountered in some amputations at the knee joint.

Amputations through the supracondylar region of the femur are best made with a long anterior flap and a posterior scar. A large degree of end bearing is provided by the osteoplastic method of Gritti-Stokes and by the tendinoplastic methods of Callander and of Kirk. The English experience with a large number of osteoplastic amputations performed between 1914 and 1918 shows that most of these stumps have broken down after some years and been reamputated at a higher level. The composite experience of American limb manufacturers shows that whenever the technical details of the operation were carried out originally the incidence of reamputation has been very small. The tendinoplastic procedures with long flaps and loose closure are particularly suitable in the presence of infection or circulatory impairment. Limb manufacturers prefer to have these stumps 3 inches shorter than the opposite femur for two reasons: to allow room for an internal knee-joint mechanism and to permit the use of a conical socket which can be entered from the top.

The physiologic factors in amputation through the shaft of the femur are similar to those through the leg. Partial end bearing is sometimes possible but most of the weight must be taken on the ischial tuberosity. Sensitiveness to the side pressure of leverage is likely to be less than in the leg because the femur is covered in its whole circumference. Muscles attaching high on the bone exert sufficient voluntary control provided the stump is long enough to transfer that motion. The prosthesis must be suspended from the shoulders or pelvis, and short stumps need a pelvic band. Function may be limited by the weight bearing surfaces available and by the instability of the flabby stump within the socket.

In amputations through the shaft of the femur the rule is to leave as much bone length as possible. The bone should be denuded of periosteum and rounded off with a rasp, as in the leg. The bone end should be covered with fascia or tendon but not with muscle. An anterior skin flap is best, though it need not be a long one to fall behind the end of the bone. Flaps should be sufficient but not redundant. An artificial limb can be applied at an early date.

In disarticulation of the hip, muscular control again becomes more difficult because one more joint is gone, but weight bearing becomes more single because the ischium, and in fact the entire buttock, can sit firmly in a bucket. Control of the entire extremity is afforded only by motions of the pelvis. Disarticulation of the hip is recommended only in case of necessity. Any thigh stump assures better function than a disarticulation. Whenever possible, sufficient muscle should be preserved to provide a cushion for bearing in an artificial leg. Such amputations can be fitted and many such legs are handled very well. It is especially important to get such an appliance early and to prohibit the postoperative use of crutches in order to avoid the crutch habit.



Sites of election for amputation with expectant function in stump.

2. UPPER EXTREMITY

The rule for amputations within the hand is to preserve every bit of every kind of tissue possible for later reconstructive surgery if necessary. This rule, however, should be modified frequently by the consideration of saving function rather than form. There is no point, for instance, in saving individual fingers which are so badly smashed that they can never be useful. The thumb falls in a different category because of its function in opposing all the fingers, so that even a stiff thumb in the opposed functional position is extremely valuable. Traumatic amputation of the tips of the fingers is well treated by immediate free full thickness skin grafts. In traumatic amputations of finger tips in which the base of the nail bed remains intact it is well to apply narrow adhesive traction strips over the end of the stump; the additional three weeks required to granulate and epithelize the wound is rewarded by a sound and sightly stump. If the entire nail bed is gone it is better to sacrifice enough bone to insure primary closure of adequate soft tissue flaps. In amputation of the middle and ring fingers a good part of the proximal phalanx must be retained in order to prevent lateral deformity of the index and little fingers developing at a later date; if the proximal phalanx cannot be retained, the distal third of the metacarpal should be removed. In loss of the little finger it is well to remove half of the meta-

carpal in an oblique fashion so as to give a smooth contour to the ulnar side of the hand. In the index finger it is probably better to leave the head of the metacarpal. In the loss of the entire thumb or of all the fingers the situation is not hopeless if function of the remaining digit or digits is retained; either thumb or fingers can be replaced by artificial members against which the remaining movable members can act. The intricate and coordinated movements of the upper extremity cannot be duplicated in artificial limbs. This limitation, for instance, is the basis for disagreement concerning the site of election for amputation about the wrist. For the application of an appliance cosmetically resembling a hand, the forearm should be amputated at the junction of the middle and lower thirds, yet the majority of patients do not wear appliances on the upper extremity and many find the heel of the hand, some movable carpal bones, or even the bulge of the styloid processes useful in movements coordinated with the other hand. In general, it is agreed that as much length as possible is desirable in all amputations in the upper extremity. A terminal scar in the arm or forearm is satisfactory.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

AT THIS YEAR'S COUNCIL MEETING THE REFEREE FOR PREPARATIONS USED NASALLY CALLED ATTENTION TO THE INCREASING NUMBER OF REPORTS OF LIPID PNEUMONIA CAUSED BY THE USE OF OILY PREPARATIONS IN THE NOSE. AS A RESULT OF THE ENSUING DISCUSSION THE COUNCIL ASKED DR. PAUL R. CANNON TO PREPARE A PAPER ON THIS SUBJECT. DR. CANNON KINDLY CONSENTED AND THE COUNCIL ADOPTED THE APPENDED REVIEW FOR PUBLICATION.

PAUL NICHOLAS LEECH, Secretary.

THE PROBLEM OF LIPID PNEUMONIA

A BRIEF REVIEW

PAUL R. CANNON, M.D.
CHICAGO

It is now fifteen years since Laughlen [1] called attention to a type of pneumonia caused by the aspiration into the lungs of oily medicaments administered either intranasally or by mouth. Of the several names which have been applied to the condition, such as lipoid pneumonia, lipid pneumonia, fat pneumonia, steatosis of the lungs, pneumonoliposis, lipoid cell pneumonia, paraffin pneumonia, oil pneumonia and oil aspiration pneumonia, "lipid pneumonia," suggested recently by Graef,[2] seems to be the most appropriate. Although many phases of the subject have been clarified [3] in the twenty-two or more papers which have been published in this country alone, the fact that so many unsuspected cases continue to be discovered at necropsy suggests that many persons, including physicians, are still unfamiliar with the conditions leading to its development.

The pneumonia varies greatly in severity, depending on the kinds and amounts of lipids aspirated. Some oils are markedly irritating and cause an acute edema and alveolitis with accompanying symptoms of cough and increased respiratory rate. Massive aspirations of oil have led to attacks of choking, cyanosis and suffocation, caused by the accumulation of large amounts of oil in the alveolar spaces. Particularly serious also is the septic pneumonia which so frequently follows the aspiration of the lipid, owing presumably to the concomitant entrance into the lungs of the irritating oil and pathogenic micro-organisms. This condition is usually accompanied by fever and a persistent cough. In many instances of aspiration of lipids, however, the pulmonary damage is minimal and the symptoms are correspondingly slight or absent. This is particularly true when small amounts of liquid petrolatum enter the lungs. The harmful effects here result from the repeated entrance of the oil into the lungs, its accumulation in the air spaces and its prolonged irritating effect. This form of lipid pneumonia is serious because its development is so insidious. Finally, there are instances of lipid pneumonia in which diagnosis is made only by microscopic examination of the lungs. The demonstration of a few collections of lipophages in alveoli is obviously of little importance in itself; the real value of the observation lies in its proof of the ease with which light oils and fluids can pass from the upper respiratory passages to the lungs. This is perhaps the most important lesson which the study of lipid pneumonia has revealed.

OCCURRENCE AND PATHOGENESIS

Lipid pneumonia may occur whenever exogenous lipids enter the pulmonary tissues and remain there long enough to cause irritation. Its pathogenesis is the most important feature of the subject, because the disease can be prevented only by knowing what types of lipids enter the lungs and under what conditions.

The lipids most commonly concerned are of two main kinds: (1) those taken by mouth and (2) those introduced into the upper respiratory passages. The first group includes cod liver or halibut oil, castor oil, liquid petrolatum or milk fat; the second group comprises the various medicated oils that are used as intranasal sprays or nose drops. Some cases have been reported in which liquid petrolatum was used as a lubricant after tracheotomy or laryngectomy,[4] and Garvin [5] has reported an instance in which the patient allowed an oily salve to trickle down the throat daily over a period of about one month. In the cases reported by Davis [6] and Houck,[7] medicated liquid petrolatum was instilled directly into the trachea, and in one case the oil was used as a nasal douche, three or four times a day, over a period of nine years. It was estimated that during this time the patient had used more than 9 gallons of liquid petrolatum!

The earlier reports on the occurrence of lipid pneumonia led to the belief that it is essentially a disease of infants and children. Accumulated evidence has proved, however, that it affects all ages, and at least 105 cases, most of which were discovered at necropsy, have been reported in adults.[8] The view, furthermore, that it occurs almost entirely in weakened individuals and particularly in those with defects of deglutition is no longer correct; it is now certain that healthy persons may develop severe types of lipid pneumonia, especially

From the Department of Pathology, the University of Chicago.

1. Laughlen, G. F.: Studies on Pneumonia Following Naso-Pharyngeal Injections of Oil, Am. J. Path. **1**: 407-414 (July) 1925.

2. Graef, Irving: Studies in Lipid Pneumonia, Arch. Path. **28**: 613-667 (Nov.) 1939.

3. Pinkerton,[2a] Ikeda,[2b] Freiman, Engelberg and Merrit.[8]

4. Ellinger, E.: Paraffinölschadigung der Lunge, Fortschr. a. d. Geb. Röntgenstrahlen **49**: 397-403 (April) 1934. Brenner, F., and Urban, F. F.: Zur Kenntnis der "Paraffinlunge," Wien. klin. Wchnschr. **50**: 1248-1251 (Sept. 3) 1937.

5. Garvin, C. F.: Lipoid Pneumonia: Report of Two Cases, Arch. Int. Med. **64**: 586-589 (Sept.) 1939.

6. Davis, K. S.: Roentgenographic Changes Following the Introduction of Mineral Oil in the Lungs, Radiology **26**: 131-137 (Feb.) 1936.

7. Houck, G. H.: Pulmonary Oil Tumors: Granulomata Caused by the Intratracheal Instillation of Liquid Petrolatum (Lipoid or Oil Aspiration Pneumonia), with Report of a Case, Medical Papers Dedicated to Henry Asbury Christian, Baltimore, Waverly Press, 1936, pp. 463-478.

8. Freiman, D. G.; Engelberg, Hyman, and Merrit, W. H.: Oil Aspiration (Lipoid) Pneumonia in Adults. A Clinicopathologic Study of Forty-Seven Cases, Arch. Int. Med. **66**: 11-38, July, 1940.

if they use medicated liquid petrolatum intranasally in large quantities over long periods of time.

Aspiration of milk fat, fish oil or liquid petrolatum may occur under conditions which are difficult or at times impossible to control, as, for instance, in babies or debilitated adults who are recumbent for long periods of time. Aspiration of these lipids is further favored by conditions which interfere with normal processes of deglutition, such as cleft palate, convulsions, spasms, frequent attacks of gagging or vomiting, cerebral birth injuries and congenital neurologic disorders. Similarly, in adults who use liquid petrolatum for the relief of constipation, pulmonary aspiration may be favored by dysphagia caused by nervous disorders, cerebral hemorrhage, brain tumors, or by local inflammations or neoplasms of the mouth, throat, larynx or esophagus.

Of particular interest, because it is more easily controlled, is the type associated with the intranasal use of medicated liquid petrolatum. This form of therapy is widespread, not only in medical practice, but also in home medication. Although physicians are beginning to discourage the custom, many persons continue to use the "nasal oils" because of the extensive advertising campaigns of the makers. One company, over the radio, urges every one with symptoms of a beginning cold to put "a few drops in each nostril" when needed. No warning is given as to the possible harm resulting from their excessive or habitual use. Abandonment of this type of medication will be slow because of the fact that so many persons have used oily nose drops with no apparent ill effects. This, however, no more indicates the harmlessness of the practice than does the occasional ingestion of small amounts of lead prove that it is not a poison and can therefore be eaten repeatedly over a long period.

It is particularly regrettable that liquid petrolatum was selected as the solvent for various medicaments in the treatment of infections of the upper respiratory tract. This oil was chosen mainly because of the belief that it is "bland," is nonirritating, does not become rancid, spreads easily, and prevents drying and crusting of the respiratory surfaces. It was not realized how readily the oil, under certain conditions, can enter the lungs and that the persistent use of a few drops a day over a period of days and weeks can lead to the entrance of considerable quantities. Walsh and Cannon [9] have cited the directions given by one manufacturer that "for children from six months to ten years of age the dosage is one-half dropperful in each nostril three or four times a day." As this dropper contained 1.5 cc., a six months old child would receive a total dose of from 4.5 to 6 cc. a day, or more than an ounce a week. If only a third of this got into the small lungs of a baby, a large area of pulmonary tissue would necessarily be affected. The most unfortunate aspect of the problem, however, is the fact that liquid petrolatum cannot be metabolized by tissue enzymes as can some of the animal and vegetable oils and hence remains as a foreign body irritant. This effect in subcutaneous tissues is well known as the so-called paraffinoma. Its similar effect in the pulmonary tissues caused Ikeda [10] to designate this type of lipid pneumonia "paraffinoma of the lung."

MODE OF ENTRANCE INTO THE LUNGS

Liquid petrolatum, either when instilled or when sprayed into the nostrils, may enter the lungs in varying amounts, depending on the dosage, the frequency with which it is applied and the extent to which the epiglottis functions effectively. It reaches the lungs fairly easily, however, because, being light, it does not elicit the cough reflex but enters the glottis and is aspirated or allowed to gravitate into the alveolar spaces. This is especially likely to happen during sleep if the oil has been used before retiring, as shown by the demonstration by Quinn and Meyer [11] that iodized poppy-seed oil instilled into a patient's nose during sleep could be readily demonstrated in the bronchial tree. Although probably only a small proportion of the oil enters the lungs, the remainder being swallowed, long-continued use may lead, eventually, to its accumulation in considerable quantities, because, once within the alveolar spaces, comparatively little resorption apparently occurs. This fact is strikingly shown in the case reported by Fischer-Wasels [12] of a 70 year old woman who was thought to have a tumor of the lungs. At necropsy, however, it was discovered that the supposedly neoplastic masses contained large quantities of a nonsaponifiable oil. Inquiry revealed that this woman, for many years, had had the daily habit of spraying her nasal passages with large amounts of a mentholated liquid petrolatum. Similar cases have since been reported.[13] Fischer-Wasels suggested that the menthol in these preparations may act as a mild local anesthetic and thus lessen the tendency for the cough or gag reflex to prevent the entrance of the oil into the trachea.

PATHOLOGIC EFFECTS IN THE LUNGS

The effects of this entrance of foreign lipids may be acute or chronic, localized or diffuse. The oils are all irritating, although in varying degree, and may cause inflammatory changes ranging from simple congestion and edema to necrosis. Pinkerton [14] demonstrated quite clearly that the animal oils, particularly cod liver oil, are highly irritating, whereas some of the vegetable oils, such as olive oil, cottonseed oil, sesame oil and poppy-seed oil, are relatively nontoxic. This blandness of vegetable oils is of practical importance in that iodized poppy-seed oil has been so useful in bronchography and has apparently led to no serious aftereffects in the lungs.[15] Pinkerton suggested that the greater tissue-damaging effect of the animal oils may be due to their greater hydrolytic cleavage into irritating fatty acids. He observed, however, that chaulmoogra oil is markedly toxic to pulmonary tissues, and Graef [2] has recently pointed out that several of the vegetable oils, notably croton oil, castor oil and peanut oil, are exceedingly active tissue irritants. There is no doubt, however, that cod liver oil is extremely injurious to pulmonary tissues and its aspiration has been followed by severe cases of lipid pneumonia, some even with abscess formation.[16]

Liquid petrolatum, although less acutely damaging than the aforementioned oils, is far from bland. Experiments performed by Cannon and Walsh [17] showed that

9. Walsh, T. E., and Cannon, P. R.: The Problem of Intranasal Medication, Ann. Otol., Rhin. & Laryng. **47:** 579-607 (Sept.) 1938.
10. Ikeda, Kano: Lipoid Pneumonia of the Adult Type (Paraffinoma of the Lung), Arch. Path. **23:** 470-492 (April) 1937.
11. Quinn, L. H., and Meyer, O. O.: The Relationship of Sinusitis and Bronchiectasis, Arch. Otolaryng. **10:** 152-165 (Aug.) 1929.
12. Fischer-Wasels, B.: Tödliche Lungenschrumpfung durch Gebrauch von Mentholöl, Frankfurt Ztschr. f. Path. **44:** 412-425, 1933.
13. Gaertner, K.: Ueber Paraffingranulome in der Lunge, Frankfurt. Ztschr. f. Path. **51:** 98-103, 1937. Ball, F. E.: Petrolatum Oil Pneumonia in An Adult, Illinois M. J. **69:** 62-65 (Jan.) 1936. Bodmer, H., and Kallós, P.: Ueber schwere Lungenschädigung (Lungenzirrhose) infolge Aspiration von Paraffinöl bei therapeutischer Anwendung, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **136:** 40-45, 1933. Bishop, P. G. C.: Oil Aspiration Pneumonia and Pneumolipoidosis, Ann. Int. Med. **13:** 1327-1359 (Feb.) 1940. Walsh and Cannon,[9] Thomas and Rienhoff.[32]
14. Pinkerton, Henry: The Reaction to Oils and Fats in the Lung, Arch. Path. **5:** 380-401 (March) 1928.
15. Wright, R. D.: Reaction of Pulmonary Tissue to Lipiodol, Am. J. Path. **11:** 497-501 (May) 1935.
16. Cannon, P. R.: Lipoid Pneumonia, Arch. Path. **19:** 135-136 (Jan.) 1935.
17. Cannon, P. R., and Walsh, T. E.: Lipoid Pneumonia and Some Potential Dangers of Intranasal Medication, Internat. Clin. **3:** 109-115 (Sept.) 1938.

the intranasal instillation of purified liquid petrolatum into healthy rabbits caused the development of acute pulmonary edema, proving that the oil in the lungs can injure capillaries sufficiently to cause increased capillary permeability and the leakage of albumin into the alveolar spaces. This fact has a definite bearing on the intranasal use of medicated liquid petrolatum in infants and young children with acute infections of the upper part of the respiratory tract. Under these conditions it is probable that whatever oil enters the lungs carries with it bacteria or viruses, and these, because of the edema induced by the oil, may find conditions more favorable for development, thus initiating a bronchopneumonia. In case of death all evidence of the early injurious effects of the oil in setting the stage for the terminal pneumonia might easily be obscured by the abundant inflammatory exudate.

The chronic effects in the lungs from the aspiration of liquid petrolatum are particularly severe, owing to the fact that it leads to the development of reticulum fibers, giant cells and, in time, abundant fibrosis. The subsequent formation of scar tissue is, consequently, as destructive to pulmonary integrity as is any other fibrosing process. It is likely, furthermore, to be more insidious, because the resultant persistent cough may lead to the more frequent use of nasal sprays or instillations in a further attempt to alleviate the cough.

Although the effects from the aspiration of oils are confined for the most part to the lungs and tracheobronchial lymph nodes, instances of blood stream dissemination are recorded [18] in which liquid petrolatum has been found as encapsulated masses of oil giving the appearance of tubercle-like lesions in the spleen and liver. In the case reported by Young, Applebaum and Wasserman [19] in which cod liver oil had been aspirated, renal lesions suggestive of periarteritis and diffuse glomerular nephritis were attributed to embolic blockage by oil droplets.

Microscopic demonstration of the presence of oily materials is usually simple although the differentiation of the kinds, and the determination whether they are endogenous or exogenous, is more difficult. With exogenous lipids the alveolar spaces are filled characteristically with large vacuolated mononuclear cells which at times have almost a signet-ring appearance. These so-called lipophages fill many air spaces and may at times be coughed up and identified in smears of the sputum. Liquid petrolatum can be partially identified by the fact that it stains with scarlet red but does not reduce osmic acid. It is also insoluble in absolute alcohol. Cod liver oil, on the other hand, reduces osmic acid and, as emphasized particularly by Pinkerton, forms characteristic acid-fast membranes at the edges of the oil masses which can be demonstrated by the Ziehl-Neelsen method. More complete and accurate identification of the oils is best made by chemical extraction of tissues, with subsequent determination of boiling points, iodine number, degree of saponification, acrolein reaction and specific color reactions. By these methods Pinkerton, Graef and Freiman, Engelberg and Merrit, particularly, have clarified several important details of the general problem. Similar chemical studies will add much valuable information concerning pathogenesis of lipid pneumonia in individual cases.

18. Pinkerton, Henry, and Moragues, Vicente: Paraffinoma of the Lung with Secondary Tubercle-like Lesions in the Liver and Spleen, Arch. Path. **29**: 691-699 (May) 1940. Pinkerton.[2] Young, Applebaum and Wasserman.[19]

19. Young, Anna M.; Applebaum, H. S., and Wasserman, P. B.: Lipoid Pneumonia: Report of a Case, J. A. M. A. **112**: 2406-2409 (June 10) 1939.

DIAGNOSIS

The diagnosis of lipid pneumonia, although usually not made ante mortem except in the severer cases, is possible at times. Of first importance is the history of the use of oily materials by mouth or in the nasal passages, with information as to amounts, duration and frequency of use. A persistent cough may be present, and in some instances there has been a history of choking attacks. Periods of low grade fever, due presumably to an accompanying septic pneumonia, have been observed. These symptoms, in conjunction with the physical observation of impaired pulmonary resonance and altered breath sounds, are informative, particularly if observed in a weak, debilitated or premature infant and in infants or adults with dysphagia from any cause.

Laboratory aids to diagnosis include the demonstration of oil laden macrophages in coughed up sputum or in tissue obtained by the bronchoscope for biopsy. Roentgenologists [20] have added considerably to the means of diagnosis by their demonstration of areas of increased density in the posterior, dependent portions of the lungs and in the perihilar regions with a tendency to be more marked on the right side. It is obvious, however, that these effects are evident mainly in patients with extensive and chronic involvement. Roentgenologists also emphasize the necessity for serial roentgenograms, particularly in the moderate and mild cases.

The chronic form of lipid pneumonia, especially that due to liquid petrolatum, must be differentiated from such conditions as pneumoconiosis, chronic bronchitis or bronchiectasis, chronic asthma, passive congestion, unresolved pneumonia, chronic fibroid tuberculosis, fungous infections of the lungs and bronchogenic carcinoma. Accurate differentiation is especially important with respect to the latter condition because of the increasing employment of surgery in its treatment. Errors in diagnosis here are particularly serious and, indeed, have already occurred. Rigler [21] reported a case of unilateral lipid pneumonia in an adult which was diagnosed as bronchogenic carcinoma, and in the case reported by Thomas and Rienhoff [22] pneumonectomy was performed on a 35 year old man on whom a diagnosis of carcinoma of the lung had been made. Death occurred from infection a few days later and the necropsy revealed a localized lipid pneumonia of the middle lobe of the right lung. It was learned later that "for over three years it had been the habit of the patient to apply medicated nasal spray with an atomizer, especially at night before retiring. The spray consisted of liquid petrolatum containing menthol and ephedrine." As so many adults are using oily nose drops and sprays by self medication, thoracic surgeons will need to give serious attention to the possible presence of chronic lipid pneumonia in the differential diagnosis of carcinoma of the lung.

INCIDENCE

It is impossible at present to ascertain the incidence of lipid pneumonia, and only certain inferences can be drawn from the evidence now available. The clinical effects vary greatly because of the different types and amounts of oils aspirated and, except in the severer cases, clinical diagnosis is therefore difficult. Most of the cases reported have been diagnosed at necropsy;

20. Pierson, J. W.: Some Unusual Pneumonias Associated with Aspiration of Fats and Oil in Lungs, Am. J. Roentgenol. **27**: 572-579 (April) 1932. Brown, R. S., and Wolman, I. J.: Lipoid Pneumonia in Infants and Children, Radiology **32**: 1-7 (Jan.) 1939. Davis.[8]

21. Rigler, Leo, in discussion on Davis.

22. Thomas, H. M., Jr., and Rienhoff, W. F.: Lipoid Cell Pneumonia, Adult Type, South. M. J. **32**: 1077-1080 (Nov.) 1939.

there are, no doubt, many more that have been overlooked or left unreported by pathologists. It is obvious that postmortem evidence alone can tell but little about the incidence of many kinds of disease. This is important to bear in mind because many physicians feel that, as so few necropsy cases have been reported, lipid pneumonia is a rare disease. By such logic, however, one would have to conclude that many diseases are rare, as for example morphinism, vitamin B deficiency or allergy. As the mild cases of lipid pneumonia are usually unsuspected, it is probably a more common malady than the nearly 200 cases which have been reported would indicate.

Furthermore, the incidence of lipid aspiration will vary directly with the extent to which pathologists make systematic routine histopathologic examinations of the lungs in every necropsy. Pinkerton [23] found 6 instances in 290 consecutive necropsies of infants and young children; Ikeda [24] found 7 in 101 consecutive necropsies. Freiman, Engelberg and Merrit,[8] in attempting to ascertain the incidence among elderly patients with chronic disease, found 41 instances in 3,500 consecutive necropsies. We have found 39 instances in 2,000 consecutive necropsies, of which 12 were of infants and children and 27 of adults. These figures give a rough idea of the extent to which lipids may be aspirated, but it is obvious that the incidence of this aspiration must vary widely in different parts of the country and of the world, depending on the distribution of respiratory infections and the tendency of physicians and of the public to use medicinal oils.

PREVENTION

Lipid pneumonia, being essentially a man-made disease, can be prevented largely by the extent to which the conditions now known to favor its development are eliminated. In infants greater care can be paid to methods of administering fish oil and liquid petrolatum in order to avoid the hazards of aspiration, as for instance by the giving of smaller amounts per dose or by using concentrates. One of the great hazards can be removed by the elimination of all forcible feeding of cod liver oil or liquid petrolatum. The disastrous consequences of this practice have already been mentioned. Monfort [25] cites a case in which a 7 weeks old child in good health was forcibly given liquid petrolatum while crying. Soon after, the child developed a hacking cough, rapid respiration (86-88 per minute) with periods of apnea and with normal temperature and blood count. Roentgenograms revealed extensive bilateral infiltration in the hilar spaces. Eleven days later death resulted from bronchopneumonia. Greater care can also be given to the feeding of prematurely born or to weakened or debilitated infants.[26] Pinkerton warned against the practice of feeding such infants while lying on their backs, and Monfort has called attention to the need for abandoning the not uncommon practice of propping the nursing bottle on a pillow with the nipple remaining in the mouth. It is probable, therefore, that some cases of lipid aspiration can be prevented by giving more attention to these and other causative factors such as the feeding of comatose individuals, the use of gavage and the prevention and control of vomiting.

The problem of prevention of lipid pneumonia due to intranasal medication is more hopeful. Of the cases in adults thus far reported in the literature, approximately 20 per cent were acquired because of intranasal medication, and in a series of cases including infants, children and adults, reviewed by Walsh and Cannon, approximately a third resulted from intranasal medication. It would seem advisable, therefore, to reexamine the rationale of local medication of the upper part of the respiratory tract in order to ascertain whether the benefits which may result from this mode of therapy outweigh the harmful effects now so well demonstrated in the massive natural experiment of lipid pneumonia.

Heatly,[27] in discussing recently the problem of therapy in acute rhinitis, said "The ideal therapeutic aims of local medication in acute rhinitis are the reduction of nasal congestion, the promotion or restoration of ciliary function and the destruction of pathogenic organisms." He cited evidence from the work of Proetz,[28] Lierle and Moore [29] and Fenton and Larsell [30] that many of the commonly used nasal oils and so-called antiseptics actually impair or paralyze ciliary activity and even destroy respiratory epithelium. Walsh and I [9] have discussed elsewhere the general problem of intranasal medication and have challenged the assumption that the solution of medicaments in liquid petrolatum possesses any advantage over aqueous solutions containing dextrose or sodium chloride. We have also questioned the generally held opinion that such antiseptics as menthol, eucalyptol, guaiacol or iodine, when dissolved in oil or in any other solute, can exert any important bactericidal action on bacteria or viruses developing in or beneath the nasal mucosa. Scientific proof, not personal opinion of the physician or patient, is necessary before we can rightly conclude that any of these exert a genuinely effective antibacterial or antiviral action. If only symptomatic anticongestive effects are aimed at by local medication, these can be as well secured by the use of aqueous solutions, thus avoiding the real dangers associated with the use of irritating oils. Statements that these intranasal preparations exert a "stimulating," "healing" or "bactericidal" effect should not be accepted until there is some objective evidence as to their validity. At present there is considerable evidence to the contrary. As Proetz [31] has recently said in stressing the importance of the functional point of view in rhinology and the need for reexamination of therapeutic methods empirically employed, "It is likewise progress, though it seldom occurs to us to abandon old methods . . . when they have been discredited. Not to abandon them after they have been proved harmful is reprehensible."

No argument is necessary regarding the need for additional information about the therapy of infections of the upper part of the respiratory tract. Too much trust, however, has hitherto been placed on empiric treatment rather than controlled observation. As a result, the public has accepted this attitude, and self medication with nasal oils is widespread. It is not likely that this will be stopped until the medical profession takes the leadership in the educational campaign to eliminate the practice.

23. Pinkerton, Henry: Oils and Fats: Their Entrance into and Fate in the Lungs of Infants and Children—A Clinical and Pathologic Report, Am. J. Dis. Child. **33**: 259-285 (Feb.) 1927.
24. Ikeda, Kano: Oil Aspiration Pneumonia (Lipoid Pneumonia), Am. J. Dis. Child. **49**: 985-1006 (April) 1935.
25. Monfort, J. A.: Lipoid Pneumonia, M. Times **67**: 320-325 (July) 1939.
26. Goodwin, T. C.: Lipoid Cell Pneumonia, Am. J. Dis. Child. **48**: 309-326 (Aug.) 1934.
27. Heatly, C. A.: Local Medication of the Upper Respiratory Tract, J. A. M. A. **107**: 1887-1889 (Dec. 5) 1936.
28. Proetz, A. W.: Effects of Certain Drugs on Living Nasal Ciliated Epithelium, Ann. Otol., Rhin. & Laryng. **43**: 450-463 (June) 1934.
29. Lierle, D. M., and Moore, P. M.: Effects of Certain Drugs on Ciliary Activity of the Mucosa of the Upper Respiratory Tract, Arch. Otolaryng. **19**: 55-65 (Jan.) 1934.
30. Fenton, R. A., and Larsell, Olof: An Experimental and Clinical Study of Histiocytes in Acute and Chronic Inflammation of the Accessory Sinuses, Laryngoscope **43**: 233-241 (April) 1933.
31. Proetz, A. W.: Functional Point of View in Rhinology, J. A. M. A. **115**: 421-422 (Aug. 10) 1940.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET - - - CHICAGO, ILL.

Cable Address - - - - "Medic, Chicago"

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SATURDAY, DECEMBER 21, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

VIRUS STUDIES IN A NEW RESPIRATORY INFECTION

Many reports have appeared recently concerning an acute infectious disease of the respiratory tract in man, associated with unusual pathologic changes in the lungs. Sporadic cases as well as minor epidemics have been described occurring in various parts of the United States and abroad (England, France, Hawaii, Spain). The disease has been described under a variety of names, such as acute influenza pneumonitis (Bowen), acute pneumonitis (Allen), atypical pneumonia (Cass), acute interstitial pneumonitis (Smiley and others), bronchopneumonia (Miller and Hayes), atypical bronchopneumonia (Murray), circumscribed pneumonia and disseminated focal pneumonia. All these terms are too restrictive, since they describe pulmonary changes observed only in the more severe cases. The majority of the cases do not present these changes. Furthermore, the terms fail to throw any light on the etiology of the infection. The disease differs from the familiar forms of lobar pneumonia caused by pneumococci and from bronchopneumonia caused by the hemolytic streptococcus, staphylococcus, Pasteurella tularensis and the forms accompanying acute infectious diseases of infancy and childhood.

Reimann [1] in 1938 described a series of 8 cases of an unusual, uniform, severe infection of the respiratory tract. The disease occurred in adults and began as a mild infection. This was followed by severe, diffuse atypical pneumonia and in the 2 fatal cases by symptoms of encephalitis. Dyspnea, cyanosis, cough without sputum, drowsiness and profuse sweating were the chief characteristics. Blood cultures remained sterile, and agglutinins for other bacillary diseases were absent. Kneeland and Smetana [2] reported 52 cases of atypical bronchopneumonia observed within the past two years at the Presbyterian Hospital, New York. The course of the infection was characterized by an insidious onset, a normal or only slightly elevated leukocyte count early in the disease, a sputum entirely comparable from a bacteriologic standpoint to that of healthy persons. The pulmonary consolidation was incomplete and tended to be migratory. Most of the cases were mild. The more severe cases presented a prolonged course, a tendency to relapse, cyanosis with obstructed breathing and leukocytosis late in the disease. Sulfapyridine had no antipyretic effect nor any effect on the course of the disease. The microscopic features of the pneumonia in the 1 fatal case were likewise unusual and were characterized by a mononuclear cell exudate and an acute pulmonary vasculitis.

There is abundant evidence to show that the disease is readily transmissible. Most of the reports refer to the occurrence of the disease among college students or in garrisoned troops. Miller and Hayes [3] reported a small epidemic at the University of Oregon. Smiley, Showacre, Lee and Ferris [4] reported a series of 86 cases occurring in a fifteen month period among the students at the Cornell University, while Maxfield [5] reported a similar epidemic involving 63 cases of "atypical leukopenia pneumonia" seen at the Baylor Hospital, Dallas, Texas. Longcope [6] points out that more than half of the 32 cases of this particular variety of pulmonary disease observed by him at the Johns Hopkins Hospital occurred during October, November and December, whereas pneumococcic pneumonia is most prevalent in Baltimore from December to May, a period

1. Reimann, H. A.: An Acute Infection of the Respiratory Tract with Atypical Pneumonia, J. A. M. A. **111**: 2377 (Dec. 24) 1938.
2. Kneeland, Y., Jr., and Smetana, H. F.: Current Bronchopneumonia of Unusual Character and Undetermined Etiology, Bull. Johns Hopkins Hosp. **67**: 229 (Oct.) 1940.
3. Miller, F. N., and Hayes, Marian G.: Bronchopneumonia of Mild Severity at the University of Oregon, Northwest Med. **38**: 12 (Jan.) 1939.
4. Smiley, D. F.; Showacre, E. C.; Lee, W. F., and Ferris, H. W.: Acute Interstitial Pneumonitis, J. A. M. A. **112**: 1901 (May 13) 1939.
5. Maxfield, J. R.: Atypical Pneumonia with Leukopenia, Texas State J. Med. **35**: 340 (Sept.) 1939.
6. Longcope, W. T.: Bronchopneumonia of Unknown Etiology, Bull. Johns Hopkins Hosp. **67**: 268 (Oct.) 1940.

during which only 8 of his 32 cases were encountered. The onset of the disease was similar in most of the cases, but the subsequent course varied greatly from a mild infection to one which was extremely grave or fatal. There was a moderate leukopenia in the beginning, the leukocytes rising in the later stage, seldom, however, higher than 13,000 and without a corresponding increase in the polymorphonuclear neutrophilic leukocytes. Frequently repeated blood cultures were negative, as were agglutinin reactions for Pasteurella tularensis, Brucella abortus and Salmonella suipestifer. Among the features which distinguish this infection as a disease entity Longcope points out the onset with high fever, headache, sweating, rasping, nonproductive cough that may become paroxysmal, the meager physical signs of consolidation of the lungs with spotty or dense shadows in the roentgenograms, the normal or slightly elevated leukocyte count and the infrequency of chill, pain in the chest and rusty sputum. The persistence of signs and symptoms for seven to fourteen days even in the mild cases and the prolonged course lasting three weeks or more in the severest infections form a striking feature. The disease presents many features which in Longcope's opinion suggest that it might be caused by a filtrable virus. These are its contagiousness, the long incubation period, the inability to demonstrate by culture of the sputum or of blood or by agglutination reactions that it is associated with any known pathogenic bacteria, and, finally, the peculiarity of the pathologic changes consisting of a mononuclear cell exudate into the pulmonary alveoli. Reimann and Havens [7] describe an outbreak of an epidemic disease of the respiratory tract which occurred in Philadelphia in 1939. Of a group of 813 persons in the personnel of the Jefferson Medical College and Hospital 50 per cent were ill. Eighty-eight per cent of the patients were ill with nasopharyngolaryngitis, 6 per cent had tracheobronchitis and 6 per cent had tracheobronchopneumonia. The disease resembled epidemic influenza in many respects but was caused by a different agent. These authors call attention to the fact that, from the standpoint of public health, mild infections are all potentially dangerous. They may be the precursors of an outbreak of a more serious disease of the respiratory tract caused by the invasion of bacteria like that which occurred in 1918-1919 after influenza. Reimann believes that the failure to isolate a virus of these cases was probably due to the delay before attempts were made or to the weak pathogenicity of the virus for the species of animals which were inoculated. With only 2 patients of his first series [1] attempts were made to obtain a virus as early as the fourth day of illness. From both patients Dr. Stokes [8] and Dr. Francis obtained an unusual virus from the nasopharyngeal washings of one and from the blood of the other. It was equally virulent for mice and caused pneumonia and encephalitis about two weeks after inoculation. Unfortunately, however, the agent was lost before serologic tests could be done. Consequently evidence was not obtained regarding any etiologic relationship. Now Weir and Horsfall [9] report unsuccessful attempts to infect a variety of animals such as ferrets, mice, guinea pigs, rabbits, monkeys, opossums, skunks, woodchucks, voles, deer mice and Syrian hamsters by intranasal inoculation with throat washings from a number of clinically typical cases. They took the infectious material to Kingston, Jamaica, in order to attempt to transmit the infection to the wild mongoose. The abundance of this animal in some of the Caribbean islands and the resemblance to the ferret were the chief reasons for this choice. They have succeeded in recovering a virus capable of producing pulmonary consolidation in this animal. The virus was filtrable through Berkefeld V and N candles, was not inactivated by glycerin or by freezing and drying in vacuum, and was propagated for at least thirty serial passages on the chorio-allantoic membrane of the developing chick embryo. Normal mongooses placed in contact with infected mongooses developed pulmonary consolidation. The virus was neutralized by the serum of mongooses convalescent from the infection but was not neutralized by normal mongoose serum. Serum of human beings convalescent from acute pneumonitis also neutralizes the virus, but serum obtained from the same persons during the acute phase of the disease failed to do so. The authors state that this virus is the cause of acute pneumonitis in human beings.

7. Reimann, H. A., and Havens, W. P. An Epidemic Disease of the Respiratory Tract, Arch. Int. Med. **65**: 138 (Jan.) 1940.

8. Stokes, J.; Kenney, A. S., and Shaw, Dorothy R.: A New Filtrable Agent Associated with Respiratory Infections, Tr. & Stud., Coll. Physicians Philadelphia **6**: 329 (Feb.) 1939.

9. Weir, J. M., and Horsfall, F. L.: The Recovery from Patients with Acute Pneumonitis of a Virus Causing Pneumonia in the Mongoose, J. Exper. Med. **72**: 595 (Nov.) 1940.

PULMONARY EMBOLISM IN MEDICAL PATIENTS

In the practice of surgery, pulmonary embolism has long been recognized as a frequent and important complication. Strangely, in the practice of internal medicine and in general medical practice this condition has been long neglected. Dr. Paul Dudley White,[1] of Boston, has recently reviewed twenty years of personal experience with pulmonary embolism and heart disease. The frequency of failure to recognize pulmonary embolism stresses the importance of the condition in simulating or complicating heart disease. From 1930 to 1940 he made the diagnosis of pulmonary embolism in his own practice seven times more often than in the ten year period from 1920 to 1930, though there was no essential difference either in the type of practice or in the numbers of new and old patients seen. As a matter of fact, even in the second decade the condition was largely overlooked during the first half; two thirds of the cases were seen during the last three of the total twenty

1. White, P. D.: Pulmonary Embolism and Heart Disease: A Review of Twenty Years of Personal Experience, Am. J. M. Sc. **200**: 577 (Nov.) 1940.

years. Confirmation of the diagnosis was established by undoubted clinical or necroscopic evidence. Analysis of this experience and of the postmortem reports at the Massachusetts General Hospital indicates that there has not been an abrupt increase in pulmonary embolism and infarction but that the major part at least of the supposed increase was due to greater search for and better recognition of the condition. Erroneous clinical diagnoses of bronchial or atypical lobar pneumonia, of congestive heart failure (with pulmonary edema), and even of coronary thrombosis (in a few cases) have been responsible for some of the errors of omission.

Pulmonary embolism may simulate heart disease (coronary thrombosis or congestive failure) but more often it complicates heart disease, especially mitral stenosis or congestive heart failure from any cause. Peripheral venous thrombosis is clinically evident in a minority of the cases and even concealed at necropsy in many cases unless the veins are actually explored. In some 70 per cent of the medical cases with pulmonary embolism and infarction seen post mortem, venous thrombosis, which gave little or no clinical evidence of its presence, was present in the deep veins of the legs. Sixty per cent of all cases of pulmonary embolism and infarction are in "medical" patients (half with heart disease and half without).[2] Of course, in many a case the large dilated heart allows an intracardiac thrombus in the right heart chambers to be the source of pulmonary embolism, but this actually seems to be a relatively uncommon site of origin.

Clues to the diagnosis of obscure pulmonary embolism are presented by White as follows: (1) the occurrence of unexplained fever, leukocytosis, tachycardia, faintness, prostration, dyspnea, asthma or even jaundice (from hemolysis of a large infarct plus an engorged liver), especially in a patient with heart disease (and particularly in the presence of mitral stenosis or heart failure); (2) the finding of lung signs (rales or consolidation) not adequately explained by either congestive heart failure or pulmonary infection; (3) the periodic recurrence at short intervals of episodes that individually might be mistaken for acute coronary occlusion but which in series are much more likely to mean repeated pulmonary embolism; (4) the inexplicable lack of response of a case of congestive heart failure to therapy which seemingly should be adequate (ruling out other factors such as infection, infarction elsewhere than in the lungs and thyrotoxicosis), and (5) in a few cases the characteristic electrocardiogram of the acute cor pulmonale (prominent S waves in lead 1, low, flat or even inverted T waves in lead 2, prominent Q waves and inverted T waves in lead 3 and low, flat or inverted T waves in lead 4) when the right ventricle is dilated by massive embolism (not therefore in the majority of cases of pulmonary embolism) and simulating at first glance the electrocardiogram of acute coronary thrombosis with basal infarction.

Pulmonary embolism always demands a careful search for peripheral venous thrombosis and heart disease. Its detection explains obscure signs and symptoms, refractoriness to treatment and periodic episodes of fever, tachycardia or collapse. Its presence reveals the folly of forcing unnecessarily vigorous, perhaps toxic, therapy for congestive heart failure and points to the possible help, even life saving in rare cases, to be derived from ligation of a peripheral vein.

The chief lesson to be learned from studies of important diagnostic errors of omission is the necessity to remember all the possible common causes of any given combination of symptoms and signs. Pulmonary embolism is a common cause of primary or complicating intrathoracic disease.

2. Hampton, A. O., and Castleman, B.: Correlation of Postmortem Chest Teleroentgenograms with Autopsy Findings, with Special Reference to Pulmonary Embolism and Infarction, Am. J. Roentgenol. 43: 305 (March) 1940.

Current Comment

MONGOLIAN SPOTS AND NEGRO HEREDITY

In a recent discussion[1] of a case involving rape the question of Mongolian spots as an indication of Negro inheritance received special attention. The so-called Mongolian spot is a curious manifestation of pigmentation which consists of one or more bluish dark spots that appear at birth in the sacral, lumbar and gluteal regions. These spots resemble the black and blue marks on the skin after a contusion, and, according to Dr. Carleton Simon, consulting criminologist to the Association of Chiefs of Police of the State of New York, one of the consultants in the case in question, they are more distinct the first two weeks, becoming fainter and disappearing in from two months to two years. Ninety per cent of all Japanese infants have them, and they are common also among infants of the Javanese, Malays, Chinese, natives of Greenland and tribes of the American Indian. In the Negro the Mongolian spot is rarely absent, several of the spots usually being present in the same individual. They have also been found in a few instances among Russians and the darker Mediterranean white races. Dr. Hooton, writing on the same subject, points out that the presence of Mongoloid spots is suggestive but not definitive of Negro blood and occurs also in infancy in many of the darker pigmented races. Parallel discussions of other features which have been considered as indicative of Negro blood, including physical characteristics such as increased pigment in the eyes and nails and blood tests, lead to the conclusion that there is as yet no known scientific test that will identify the racial background of a person whose blood contains so many and so dilute racial strains as to make his racial origins doubtful. Furthermore, the mathematical computation that in twenty generations every individual is the lineal descendant of

1. Bulletin, Bureau of Criminal Investigation, New York State Police, Albany 5: 6 (April) 1940.

more than a million forebears symbolizes the complicated nature of the subject. In any event, the presence of Mongolian spots alone cannot be considered to prove the presence of Negro blood in any immediate sense.

OIL ASPIRATION PNEUMONIA

Oil pneumonia, known also as lipoid or lipid pneumonia, in adults, due to liquid petrolatum, has been occurring increasingly in recent years. Errors in diagnosis may occur whereby the condition is overlooked, so that it is detected only at necropsy, if at all. Freiman and his associates [1] have shown that the aspiration of liquid petrolatum is facilitated by the fact that it is a bland drug, nonirritant to the pharyngeal mucosa and exciting no reflex inhibition. When once aspirated, gravity and inspiratory suction seem to control its disposition in the lungs. This is indicated by the fact that the lower right and left lobes are preponderantly affected. Forty-seven mostly debilitated recumbent and dysphagic patients who were suffering from some incurable disease such as carcinoma or arteriosclerosis, with an average age level of 61.8 years, had habitually used liquid petrolatum in relatively large quantities. Forty-one of these were studied at necropsy. The microscopic examination of pulmonary tissue indicates two stages in the evolution of the disease, a prompt macrophagic reaction followed by a slower process of fibrous proliferation of interstitial tissue, which eventually prevails. As fibrosis increases, cellularity diminishes. Finally there remains only a mass of hyalinized fibrous tissue with entrapped oil, a true paraffinoma. The difficulty of clinical diagnosis is increased by the absence of specific symptoms and signs. Symptoms such as cough, blood-streaked sputum, if present, pain in the chest and intercurrent fever are those associated with other forms of chronic pulmonitis. Malignant growths present elsewhere than in the lung may lead to a wrong interpretation of pulmonary shadows as metastatic in origin; but here the failure of pulmonary infiltration to increase in size over a period of months after cessation of intake of oil is strong evidence against tumoral metastasis. Laboratory data are only occasionally helpful, as the leukocyte count and the erythrocyte sedimentation rate are not affected by liquid petrolatum by itself. On the other hand, the presence in the sputum of oil globules is diagnostically valuable, if liquid petrolatum can be identified chemically or by differential staining. However, diagnosis is significantly aided by roentgenoscopy. In the early stages the markings in the lower lung fields are exaggerated. As the lesions progress, linear and nodular infiltrations develop until finally areas of consolidation are formed which are always situated at one or both pulmonary bases and which lie close to the cardiac shadow that extends from the hilus to the diaphragm. Serial roentgenograms may show no change for years other than progressive fibrosis, yet the persistence of pulmonary shadows in a patient with dysphagia receiving liquid petrolatum justifies the diagnosis of oil aspiration pneumonia. The essential features of oil pneumonia are dysphagia, a long history of intake of oil, roentgenographic demonstration of persistent, unchanging consolidations characteristically situated in the mesial portions of the bases of both lungs and complete absence of clinical evidence of pulmonary disease; but they are rarely all present. The difficulty of correct diagnosis may be illustrated by a case cited from the authors' own experience in which oil pneumonia developed during two and one-half years of hospitalization of a patient suffering with degenerative cerebellar disease, pseudobulbar palsy and dysphagia. The progress of the lesion was followed roentgenologically throughout the illness and yet the diagnosis was not established until it was too late to affect the outcome by the withdrawal of the oil. The presence of persistent pulmonary consolidations with disproportionately slight symptoms or of infiltrations which do not fit into any well established disease pattern should suggest oil pneumonia. The authors do not consider oil aspiration pneumonia a direct cause of death, unless in some extreme case, as one which fell within their experience, in which the pulmonary lesion was so extensive as to induce asphyxia. Usually the patient lives for an indefinite time and finally succumbs to his primary disease or to a secondary infection. However, purulent bronchiolitis and bronchitis, bronchiolectasis, occasionally bronchiectasis and recurring episodes of bronchopneumonia may be concomitant conditions over a considerable period. Though the use of liquid petrolatum is not necessarily productive of oil pneumonia even in the presence of some predisposing factor, it is not without potential danger. Its promiscuous use, especially by enfeebled or dysphagic persons, should be discouraged.

1. Freiman, D. G.; Engelberg, Hyman, and Merrit, W. H.: Oil Aspiration (Lipoid) Pneumonia in Adults; A Clinicopathologic Study of Forty-Seven Cases, Arch. Int. Med. **66**: 11 (July) 1940. Lipoid Pneumonia, editorial, J. A. M. A. **114**: 251 (Jan. 20) 1940.

BODY WEIGHT AND CANCER INCIDENCE

Many external factors affect the incidence of cancer. Among those recently discussed are climate, exposure to the elements, especially sunlight, and geographic location.[1] Now Tannenbaum [2] presents experimental and statistical evidence on the relation of body weight to the development of cancer. In both animals and man individuals of average or less than average weight are not as likely to develop cancer as those who are overweight, he believes. This tentative conclusion requires careful checking, and the establishment and maintenance of weight levels with a view to the prevention of human cancer can as yet be considered only as an experimental procedure. In the light of the curiously large number of correlations between cancer and internal and external factors which are now receiving attention, it is necessary to weigh all the evidence carefully and not to accept the suggestions as established until unequivocal proof has been presented.

1. Peller, Sigismund; Stephenson, C. S., and Souder, C. G.: Cancer and Its Relations to Climatic Conditions Acting During Childhood and Adolescence, Am. J. Hyg. **32**: 39 (July) 1940. Peller, Sigismund: Skin Irritation and Cancer in the U. S. Navy, Am. J. M. Sc. **194**: 326 (Sept.) 1937. Bechet, P. E.: Excessive Solar and Phototherapeutic Irradiation, Arch. Dermat. & Syph. **29**: 221 (Feb.) 1934. Craver, L. F.: Etiology of Cancer, J. A. M. A. **105**: 1820 (Dec. 7) 1935. Mountain, J. W., and Dorn, H. F.: Some Peculiarities in the Geography of Cancer, ibid. **113**: 2405 (Dec. 30) 1939.

2. Tannenbaum, Albert: Relationship of Body Weight to Cancer Incidence, Arch. Path. **30**: 509 (Aug.) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

CHANGES IN COMMITTEE CHAIRMANSHIPS OF DIVISION OF MEDICAL SCIENCES OF NATIONAL RESEARCH COUNCIL

In order to meet new and expanding requirements in the field of medical preparedness, the following changes in the chairmanships and organization of committees in the Division of Medical Sciences of the National Research Council have been announced by Dr. Lewis H. Weed, chairman of the Division of Medical Sciences:

Russell M. Wilder, Rochester, Minn., resigns as chairman of the Committee on Medicine (remains member of committee) to become chairman of the Committee on Food and Nutrition of the Division of Biology and Agriculture and of the Division of Medical Sciences.

O. H. Perry Pepper, Philadelphia, becomes chairman of the Committee on Medicine, resigned as chairman of the Subcommittee on Diagnosis and Therapeutics.

Hugh Morgan, Nashville, Tenn., becomes vice chairman of the Committee on Medicine.

James McLester, Birmingham, Ala., becomes chairman of the Subcommittee on Medical Nutrition.

Warfield T. Longcope, Baltimore, becomes chairman of the Subcommittee on Diagnosis and Therapeutics.

Henry Meleney, Nashville, Tenn., becomes chairman of the Subcommittee on Tropical Diseases vice Wilbur A. Sawyer (resigning because of duties abroad).

The complete organization was described in THE JOURNAL, November 9, page 1640.

A COMMITTEE ON FOOD AND NUTRITION TO ADVISE GOVERNMENT

The National Research Council announces the appointment of a Committee on Food and Nutrition to advise the federal government on nutritional aspects of national defense. This committee, appointed at the request of Miss Harriet Elliott, head of the Consumer Division of the National Defense Advisory Commission, will concern itself with improving the nutrition of the general population. A separate National Research Council subcommittee is already advising the Army and Navy on nutrition for these services. Several members of this subcommittee are also members of the new Committee on Food and Nutrition.

Dr. Russell M. Wilder, of the Mayo Clinic, Rochester, Minn., is chairman of the new committee. Serving with him as advisers to the government in planning its program of national nutrition for defense are specialists from agriculture, industry and science dealing with food and nutrition.

Representing the food processing industry are Mr. Cullen Thomas, executive of General Mills Corporation, Minneapolis, and Dr. Samuel C. Prescott, dean of science, Massachusetts Institute of Technology, and member of the Institute of Food Technologists. For advice on problems of food production and distribution the committee includes Dr. John N. Black, professor of agricultural economics at Harvard University. Dr. F. G. Boudreau, now executive director of the Milbank Memorial Fund but formerly head of the League of Nations technical committee on nutrition, and Dr. Joseph S. Davis, professor of economic research and director of the Food Research Institute, Stanford University, will contribute their knowledge of world food problems, as will Dr. John B. Youmans, associate professor of medicine, Vanderbilt University, who is now studying the food problems of both occupied and unoccupied France for the Rockefeller Foundation.

Advice on translating nutritional science into menus and diet lists for the welfare of the family will come to the housewife from such experts as Dr. Icie Macy Hoobler, director of research laboratory, Children's Fund of Michigan, Detroit; Dr. Helen S. Mitchell, research professor of nutrition, Massachusetts State College, Amherst, and Dr. Lydia J. Roberts, chairman of the Department of Home Economics, University of Chicago.

Specialists in certain phases of nutrition are serving on the committee. In the vitamin field a group is made up of Dr. R. R. Williams, chemical director, Bell Telephone Laboratories, who first isolated and later synthesized thiamine; Dr. George R. Cowgill, associate professor of physiologic chemistry, Yale University; Dr. C. A. Elvehjem, professor of agricultural chemistry, University of Wisconsin, and Dr. Norman Jolliffe, associate professor of medicine, New York University School of Medicine; Dr. Henry Borsook, professor of biochemistry, California Institute of Technology; Dr. Charles Glenn King, professor of chemistry, University of Pittsburgh, known for his isolation in pure form of vitamin C; Dr. Philip C. Jeans, professor of pediatrics, State University of Iowa, and Dr. W. C. Rose, professor of biochemistry, University of Illinois.

Broad as well as specialized knowledge of nutritional science will be contributed by Dr. James McLester, professor of medicine, University of Alabama, and Dr. L. A. Maynard, professor of animal nutrition and director, U. S. Plant, Soil and Nutrition Laboratory, Cornell University. Dr. McLester is chairman of the American Medical Association's Council on Foods and Nutrition and Dr. Maynard is secretary of the American Institute of Nutrition.

The committee recently held its first meeting in Washington. It gave consideration to the improvement of white flour, which is well known to be deficient in the B vitamins, necessary for health and morale, and in minerals. It will consider the possibilities of improving the quality of sugar, which likewise has been deprived of the vitamins and minerals contained in the material from which it is made—sugar cane and beets. Means will also be sought for improving the nutritional qualities of other staple foods, such as the edible fats.

It is the quality of the nation's food that is important in the present emergency, it was pointed out, whereas in the war of 1914-1918 the quantity of food was the

chief concern. It is for this reason that Miss Elliott asked for a committee of scientists to advise her, through Dr. M. L. Wilson, director of extension work, U. S. Department of Agriculture, how much of each important nutritional factor should be included in the national diet, and what things the public should be taught to eat. A national program of nutritional education is in planning, directed by Dr. Wilson.

One of the things to be taught, the committee decided at its first meeting, is that there is no detectable difference between the synthetic chemical vitamins and the natural ones. Ascorbic acid is just as good vitamin C, for example, as one gets from an orange.

Serving on the committee as liaison representatives from the American Red Cross and the United States government services will be a number of persons, several of them well known for their research in nutrition. Among those already appointed are Colonel Paul E. Howe, Dr. W. H. Sebrell, Commander Charles S. Stephenson, Dr. William DeKleine and Dr. Louise Stanley. The following authorities on nutrition have been asked to serve as advisers to Miss Elliott. They also will be asked to serve the committee as consultants: Prof. E. V. McCollum, Dr. John R. Murlin, Prof. Mary Swartz Rose and Prof. H. C. Sherman. Ex-officio members of the committee are Mr. M. L. Wilson, of the National Defense Nutrition Program, and Dr. Robert Griggs and Dr. Lewis H. Weed, chairmen, respectively, of the National Research Council's Division of Biology and Agriculture and Medical Sciences.

THE NATIONAL YOUTH ADMINISTRATION CONTRIBUTES TO THE NATIONAL HEALTH

The National Youth Administration has launched a nationwide health program to serve the needs of young workers who are employed on its out-of-school work program. This effort to afford young people the experience of practical health education in order to help strengthen the nation's vital defenses by building a strong and healthy population will be directed along three major lines:

1. A physical appraisal, by means of a technically competent health examination, of every youth assigned to an NYA job;

2. Correction of health defects through maximum utilization of community resources, through the use of supplementary medical and dental services provided where possible by the National Youth Administration and through developing in youth an interest in improving their health by their own personal efforts;

3. Improved technical advice and assistance with respect to all NYA efforts having a direct and immediate bearing on the health of youth workers, such as nutrition, sanitation, physical development and recreation.

At the September meeting of the Conference of State and Territorial Health Officers, Aubrey Williams, National Youth Administrator, outlined the purpose and scope of the out-of-school work program. Dr. Carl E. Rice, Surgeon, U. S. Public Health Service, assigned to the National Youth Administration, presented the general plans for the health program which is under his direction. The Committee on Hospital and Medical Care of this conference endorsed the proposed program in the following resolution:

WHEREAS, The health program to be initiated by the National Youth Administration is planned to promote the health and efficiency of its enrolled youths through the utilization of health and medical facilities which already exist, or may be supplemented by the National Youth Administration; and

WHEREAS, The program as planned seeks the active cooperation of state and local health departments: be it

Resolved, That the Conference of State and Territorial Health Officers endorse the principles and purpose of the National Youth Administration's health program; and

That the Conference recommend that the state health department serve, when requested, as co-sponsor of such statewide National Youth Administration health projects.

In addition to extending health services to youth, the National Youth Administration will continue through its work program to improve and extend community health facilities. During the year ended June 30, 1940, the record of accomplishment includes the production of over eight million articles of hospital supplies for public institutions, the construction of nine new hospitals and repairs and improvement to sixty-two others, the construction of forty other new buildings concerned with various health activities, and repairs and improvements on one hundred and thirty-one others. In addition, many young persons received work experience in a variety of hospital functions as ward attendants, laboratory assistants and kitchen and laundry workers.

The work program aims to acquaint young workers with modern production methods and prepares them for present employment conditions. Young men and young women gain practical work experience through employment on projects which produce useful articles, facilities and services for public agencies. Work experience in welding, sheet metal work, radio construction, automobile mechanics, wood working, sewing, book repair and office work is productive of articles for city and county departments and offices as police, welfare, health, education and sanitation.

As most of the National Youth Administration's work with unemployed young persons has a close relationship to the broad needs of defense, it has been designated as one of the National Defense agencies.

It is estimated that approximately five hundred thousand young persons out of school between the ages of 17 and 24 inclusive will be employed on the work program during the fiscal year. About 50 per cent of the persons so employed are young men. The average period of employment is less than one year. All of them come from families in the lower economic brackets. Increased employability and work productivity are important at all times, and especially at present.

One important aspect of the NYA work program, the operation of both resident and nonresident projects, influences the character of the health program. About fifty thousand young persons are employed on resident projects, where they live at the job site under NYA supervision twenty-four hours each day. In these resident projects the National Youth Administration must assume responsibility for the medical care of a comparatively small group of young persons. This is not true for the much larger group of employed young persons. The NYA health program is not a medical care program, as responsibility for providing medical care for intercurrent illnesses of the employed young persons will remain with the family or community except for the small group mentioned.

The health examination for all young persons will be made largely by designated practicing physicians. This examination follows a standard national form and includes provision for necessary smallpox vaccination, for routine serologic blood test and urinalysis, and for a routine chest roentgenogram or a routine tuberculin test followed by chest roentgenograms for positive

reactors. Everything possible is being done to assure the health education value of the examination. The examination is not regarded as a hurdle for young persons desiring to enter into NYA employment. The main purposes for giving the examination are to:

(*a*) facilitate proper work assignment;
(*b*) assist in the guidance of young persons in physical development and health education activities;
(*c*) discover health conditions that need attention.

Naturally, young persons with communicable disease, severe heart lesions or mental abnormality must be excluded. It is not intended to exclude any youth from NYA employment because of physical limitations and consequent limitations in work capacity, unless such employment will endanger the life of the individual youth or will endanger the health and safety of other young persons.

The rehabilitative effort is aimed at the correction of actual and potential health hazards and those conditions which may not be health hazards but may reduce the employment possibilities and well-being of the youth. A great part of this effort will be through influencing the young people to make their own arrangements with physicians and dentists, using a portion of their NYA wage in payment for services. This will require considerable skilful counseling with the youth concerned on the part of NYA personnel. Success will depend also on the degree of consideration and cooperation given this effort by practicing physicians and dentists. In some areas, much of the necessary follow-up work can be secured through existing community agencies if such is necessary. Such facilities, however, are usually overburdened in taking care of sick people and are not particularly desirable places to send apparently healthy persons, either for examination or for corrective work.

The National Youth Administration will establish its own facilities in some regions in connection with larger projects, utilizing the services of practicing physicians and dentists in the community on a part-time basis. Local economic conditions and the presence or absence of going health facilities will indicate the necessity for NYA supplementation.

The health of NYA employees will also be approached through activities in the field of nutrition, health information, physical training and recreation.

Each state health program will be directed by a physician of outstanding professional competence who will serve on the staff of the state administrator on a part-time basis, as health consultant, to give technical supervision and direction to all NYA health efforts. Assisting him and employed on a full-time basis to direct the statewide health project is the state health supervisor. The supervisor is usually a nonmedical person selected from the fields of public health nursing or physical education or from administrative positions in public and private health associations. Statewide health projects in every state operate in collaboration with state public health departments, which in most cases are giving material assistance in the supervision and operation of NYA health activities.

One of the main jobs of the health consultant will be to assure the wise expenditure of NYA funds. Another function will be concerned with utilizing existing health facilities to the fullest extent and securing the cooperation of practicing physicians and dentists. He will also be responsible for reviewing and making recommendations concerning medical services rendered in resident centers by physicians and dentists employed on a part-time or full-time basis.

The cooperation of the medical and dental professions will be necessary to enable the plan to succeed. As the various NYA state administrators approach officials and committees of state medical and dental societies, it is hoped that the representatives of the two professions will keep in mind that the NYA health program is primarily a practical health education effort aimed at influencing the future health practices of a group of young out-of-school unemployed persons, who will usually remain in NYA employment for only a short period.

The method of attempting to accomplish this purpose will be through imparting health information, acquainting and introducing the young people to the public and private health facilities available in their own state and community, and finally by exposing them to rehabilitative health services obtainable from the private practitioner either on the youth's own initiative or through NYA supplementation as may be indicated.

NEW CORPS AREA SURGEON

Col. Joseph E. Bastion, M. C., U. S. Army, has been announced as Corps Area Surgeon of the Sixth Corps Area with station at Chicago, to succeed Col. Paul W. Gibson, M. C., U. S. Army.

COLONEL SPRUIT ASSIGNED TO GENERAL HEADQUARTERS

Lieut. Col. Charles B. Spruit, Medical Corps, U. S. Army, who has been chief of the medical division of national headquarters, Selective Service System, since last August, has been assigned to the General Staff in the War Department and will be on duty at General Headquarters, Army War College, Washington, D. C.

NEW GENERAL HOSPITAL IN THE NORTHWEST

The War Department has announced that authority has been given for the construction of a 750 bed cantonment-type general hospital at Vancouver Barracks, Washington, to serve the military personnel in the Northwest states area. This hospital will be used in connection with existing facilities at the station hospital already at Vancouver Barracks and it is expected to be ready for occupancy early in 1941.

FORT DEVENS OFFICERS FORM SCIENTIFIC GROUP

The medical officers at Fort Devens, Mass., have formed the Society of the Medical Department Officers and have been conducting scientific meetings at the station hospital on Tuesday evenings. Beginning October 8, with an address by Lieut. A. W. Bennett on "Peptic Ulcer," the speakers have included Lieut. Miles Kelly on bronchiectasis, Lieut. Charles C. Verstandig on "Roentgen Therapy in Pneumonia," Dr. E. A. Adams, Fitchburg, Mass., "Treatment of Appendicitis," Dr. Thomas H. Ham, Boston, "Hemorrhagic Diseases and Treatment," Dr. Harry Blotner, Boston, "Diabetes Mellitus," and, December 10, Dr. Atanley J. G. Nowak, Boston, "Shock." Col. H. P. Carter has been chosen president of this group and Lieutenant Verstandig, secretary.

MEDICAL CORPS ORDERS

The following orders have recently been issued to officers of the Medical Corps of the U. S. Army:

Col. Hew B. McMurdo, from the Philippine Department to be Instructor in the Medical Corps, 33d National Guard Division, Chicago area.

Col. Joseph Casper, Winthrop, Mass., retired October 31 on account of disability incident to the service.

Capt. Francis F. Viglione, from Madison Barracks, N. Y., to the Puerto Rican Department, leaving New York November 27.

Lieut-Col. Leonard W. Hassett, from Philippine Department to Fort Slocum, N. Y.

Lieut.-Col. Lucius K. Patterson, from Panama Canal Department to Fort Riley, Kan.

Capt. Stephen C. Sitter and Capt. Edwin S. Kagy, from Washington, D. C., to the Philippine Department, sailing December 28.

Capt. Hubert T. Marshall, from Hawaiian Department to New York General Depot, New York Port of Embarkation, Brooklyn.

Capt. Edwin M. Goyette, from Carlisle Barracks, Pa., to Panama Canal Department, sailing January 18.

Capt. George F. Peer, from Panama Canal Department to New York Port of Embarkation, Brooklyn.

ARMY RESERVE OFFICERS

WAR DEPARTMENT

The following additional medical reserve officers had been ordered to extended active duty by order of the War Department, Washington, D. C., up to December 6:

ADAMO, Frank Scozzari, Lieut. Col., Tampa, Fla.
ALFORD, Thomas Dale, 1st Lieut., Little Rock, Ark.
BAUMHAUER, Charles Andrew, 1st Lieut., Whistler, Ala.
COSBY, Oswald Whitney, Captain, Baton Rouge, La.
CRAIN, Alfred Penn., Jr., 1st Lieut., Shreveport, La.
DAMROW, Harold Byran, Captain, Bristol, Va.
DAVIS, Richard Fleming, 1st Lieut., Batavia, N. Y.
DIODATI, Anthony Dominic, 1st Lieut., Philadelphia.
ELLIS, Herbert B., 1st Lieut., Raton, N. M.
HELLMAN, Jack M., 1st Lieut., Chicago.
LANDER, Herman Boris, 1st Lieut., Chicago.
McCLARY, George Robin, 1st Lieut., Miami, Fla.
MORRISSEY, Paul Gunkle, Jr., 1st Lieut., Nashville, Tenn.
POHL, Robert Leo, 1st Lieut., Spokane, Wash.
RAPALSKI, Adam Jozef, 1st Lieut., Nutley, N. J.
SHUTKIN, Manfred Ned, 1st Lieut., Milwaukee.
SPALDING, Joseph John, 1st Lieut., Indianapolis.
STERN, Robert Leo, 1st Lieut., Los Angeles.
STEWART, Magnus Jackson, Captain, Loveland, Col.
THAYER, Kent H., 1st Lieut., Phoenix, Ariz.
WINSOR, Carlton Webb, Captain, Detroit.

FIRST CORPS AREA

The following medical reserve corps officers had been ordered to extended active duty with the regular army by First Corps Area orders up to November 29. The First Corps Area comprises the states of Maine, Vermont, New Hampshire, Rhode Island, Massachusetts and Connecticut.

ARCHAMBEAULT, Armand C., Captain, Barre, Vt.
BLACK, Harry, 1st Lieut., Lowell, Mass.
CENTRONE, Patrick A., 1st Lieut., Middletown, Conn.
CINCOTTI, John J., 1st Lieut., Belmont, Mass.
CRAPOLICHIO, Dante V., 1st Lieut., Worcester, Mass.
CUMMINGS, Vincent P., 1st Lieut., North Adams, Mass.
DiPIPPO, Palmino, 1st Lieut., Providence, R. I.
FRANK, Israel R., Captain, Jamaica Plain, Mass.
LANOU, William W., 1st Lieut., Pittsfield, Mass.
LEAVITT, Benjamin, 1st Lieut., Fall River, Mass.
LEVY, William S., 1st Lieut., Woonsocket, R. I.
MAHER, Joseph P., 1st Lieut., Milton, Mass.
McIVER, Frederick D., 1st Lieut., Orleans, Vt.
NATHANS, Samuel, 1st Lieut., Hope Valley, R. I.
PEKALA, Joseph G., Captain, Northampton, Mass.
QUIGLEY, George E., 1st Lieut., Newton, Mass.
RISMAN, Joseph, 1st Lieut., Lynn, Mass.
SCHILLER, Irving W., 1st Lieut., Dorchester, Mass.
SHAPIRO, Phillip, 1st Lieut., Northampton, Mass.
SHAPIRO, Robert, 1st Lieut., Roxbury, Mass.
TIEDE, Joseph W., Major, Dedham, Mass.
WEINSTEIN, Barnett, 1st Lieut., Peabody, Mass.
WILSON, William J., Jr., 1st Lieut., Derry, N. H.
YORK, Charles L., Jr., 1st Lieut., Plymouth, N. H.

SECOND CORPS AREA

The following additional medical reserve corps officers had been ordered to active duty by the Commanding General, Second Corps Area, up to December 6. The Second Corps Area comprises the states of New York, New Jersey and Delaware.

GESSNER, Gerard R., 1st Lieut., Highland Park, N. J., 3d Military Area.
HANFLING, Seymour L., 1st Lieut., Jamaica, N. Y., 2d Military Area.
LEVINE, David, 1st Lieut., New York, 2d Military Area.
MICELI, John N., 1st Lieut., Brooklyn, 2d Military Area.
MORAN, John F., 1st Lieut., Lambertville, N. J., 3d Military Area.
PERLMUTTER, Irving K., 1st Lieut., Newark, N. J., 3d Military Area.
ROBERTS, Arthur J., 1st Lieut., New York, 2d Military Area.
ROSS, Selig J., 1st Lieut., Allendale, N. Y., 2d Military Area.
SHULMAN, Bernard H., 1st Lieut., Secaucus, N. J., 3d Military Area.

THIRD CORPS AREA

The following medical reserve corps officers had been ordered to extended active duty by the commanding general of the Third Corps Area up to December 6. The Third Corps Area comprises the states of Pennsylvania, Virginia, District of Columbia and Maryland.

CLARK, Walter Scott, Jr., 1st Lieut., Burgettstown, Pa.
DEVLIN, Laurence Patrick, Captain, Philadelphia.
DONLEY, Donald, Captain, Sharon, Pa.
NATHANSON, Leon Irving, 1st Lieut., Washington, D. C.
SHAPIRO, Abraham Albert, 1st Lieut., Baltimore.
STASKIEL, Louis Julius, Jr., 1st Lieut., Glen Lyon, Pa.

FOURTH CORPS AREA

The following additional medical reserve corps officers had been ordered to active duty by Fourth Corps Area order up to December 6. The Fourth Corps Area comprises the states of Tennessee, North Carolina, South Carolina, Alabama, Georgia, Mississippi, Florida and Louisiana.

BLACK, Paul A. L., 1st Lieut., Wilmington, N. C.
BROWN, George C., Jr., 1st Lieut., Walterboro, S. C.
CHAMBERS, Wallace L., 1st Lieut., Pickens, Miss.
DAVIS, William B., 1st Lieut., College Park, Ga.
deCAMP, Allen L., 1st Lieut., Fayetteville, N. C.
DRISCOLL, Robert H., Captain, Newberry, S. C.
EDMONDSON, Hansel E., Captain, Edwards, Miss.
FISHER, Roy A., Jr., 1st Lieut., Knoxville, Tenn.
FOURRIER, Daniel J., 1st Lieut., Baton Rouge, La.
HALL, James B., 1st Lieut., Gainesboro, Tenn.
HUSKEY, Aubrey L., Captain, Atlanta, Ga.
JORDAN, William K., 1st Lieut., Milledgeville, Ga.
KLUGH, George F., Jr., 1st Lieut., Atlanta, Ga.
McCOIN, Joseph, 1st Lieut., Lafollette, Tenn.
McGUFFIN, William C., 1st Lieut., Asheville, N. C.
MOLE, John W., Captain, Brunson, S. C.
MURPHREE, Walter E., Captain, Gainesville, Fla.
NEILL, Francis K., 1st Lieut., Albany, Ga.
NEWMAN, Lucian, 1st Lieut., Dadeville, Ala.
PROUET, Prudence E., 1st Lieut., New Orleans.
PRUSA, Victor H., 1st Lieut., Banners Elk, N. C.
RALSTON, Raymond H., 1st Lieut., Lakeland, Fla.
SPEARMAN, Walter D., Captain, Social Circle, Ga.
STEM, William A., 1st Lieut., Chattanooga, Tenn.
TANNENBAUM, Abraham J., 1st Lieut., Greensboro, N. C.
TEMPLES, Leo G., 1st Lieut., Statesboro, Ga.
WILKES, Samuel M., 1st Lieut., Laurens, S. C.

Relieved from Duty or Orders Revoked

The following officers, previously reported, have been relieved from duty or the orders have been revoked:

ARNOLD, Laurie J., Jr., 1st Lieut., Lake City, Fla.
EVANS, Milton L., 1st Lieut., Memphis, Tenn.
FERRELL, Thomas J., 1st Lieut., Waycross, Ga.
McCORD, William M., 1st Lieut., New Orleans.
VOORHIES, Norton W., 1st Lieut., New Orleans.
WORK, Samuel D., Jr., 1st Lieut., Forsyth, Ga.

FIFTH CORPS AREA

The following additional medical reserve corps officers had been ordered to active duty by Fifth Corps Area order up to November 29. The Fifth Corps Area comprises the states of Ohio, West Virginia, Indiana and Kentucky.

BONETA y RIOS, Thomas Luis Eusebio, 1st Lieut., McKee, Ky.
VEIRS, Everett Raymond, Captain, Ashland, Ky.

SIXTH CORPS AREA

The following additional medical reserve corps officers had been ordered by Sixth Corps Area Order up to December 6 to extended active duty. The Sixth Corps Area comprises the states of Wisconsin, Michigan and Illinois.

BARAK, Herbert G., 1st Lieut., Dixon, Ill.
BASSUENER, Reynold O., Captain, Warrens, Wis.
CONKLIN, James O., 1st Lieut., Paris, Ill.
DRESNER, Milton H., 1st Lieut., Chicago.
DUNN, Max Martin, 1st Lieut., Chicago.
FLORETH, Nelson K., 1st Lieut., Litchfield, Ill.
GAUTSCH, Joseph A., 1st Lieut., Decatur, Ill.
HILL, George R., 1st Lieut., Fairfield, Ill.
HOLNITSKY, Samuel C., 1st Lieut., Chicago.
HRINKO, Stephen A., Captain, Detroit.
JOHNSON, Clarence E., 1st Lieut., Hillsdale, Mich.
KALLEN, Irwin A., 1st Lieut., Chicago.
KAPLAN, Louis G., 1st Lieut., Chicago.
LOOBY, WILLIAM E., 1st Lieut., Highland Park, Ill.
LUETH, Harold C., Captain, Evanston, Ill.
MALOW, Louis, 1st Lieut., Chicago.
McCORMICK, Donald W., 1st Lieut., Madison, Wis.
MIDDLETON, John W., 1st Lieut., Detroit.
PYZIK, Stanley W., 1st Lieut., Chicago.
RECK, Lawrence E., 1st Lieut., Peoria, Ill.
ROBINSON, Ralph D., 1st Lieut., Moberly, Mo.
ROCCO, Paul Carl, Captain, Chicago.

SEVENTH CORPS AREA

The following additional medical reserve corps officers had been ordered to extended active duty by Seventh Corps Area Order up to December 6. The Seventh Corps Area comprises the states of North Dakota, South Dakota, Minnesota, Nebraska, Iowa, Kansas, Missouri and Arkansas.

ARNY, Frederick Phillip, 1st Lieut., Preston, Minn., Fort Snelling, Minn.
ATKINSON, George Stanford, 1st Lieut., White Earth, Minn., Fort Snelling, Minn.
BARTON, John Currer, Captain, Independence, Iowa, Fort Snelling, Minn.
COTTRELL, Wilson Philip, Major, Reed Springs, Mo., Fort Snelling, Minn.
ENGLISH, Wallace Davis, Captain, Cardwell, Mo., Fort Snelling, Minn.
GRAY, Herschel Frederick, 1st Lieut., Little Rock, Ark., Fort Snelling, Minn.
HAENTZCHEL, Lester Esaias, 1st Lieut., Fulton, Mo., Fort Snelling, Minn.
HANNA, Joe Tyntalinio, 1st Lieut., Omaha, Fort Crook, Neb.
HARRIS, Leon Dunham, 1st Lieut., Mobridge, S. D., Fort Crook, Neb.
HEIDRICK, Paul John, 1st Lieut., Lincoln, Neb., Fort Snelling, Minn.
HEPPERLEN, Harry Michael, Captain, Beatrice, Neb., Fort Snelling, Minn.
JOHNSON, Marvin Anthon, 1st Lieut., Plainview, Neb., Fort Snelling, Minn.
KLEVKAMP, Elmer August, Jr., 1st Lieut., St. Louis, Jefferson Barracks, Mo.
KRUMI., Joseph George, 1st Lieut., Ord, Neb., Jefferson Barracks, Mo.
LANNING, Robert Joseph, Captain, Junction City, Kan., Fort Snelling, Minn.
LEONARD, Roosevelt, 1st Lieut., Lyons, Kan., Fort Snelling, Minn.
LIPP, Frank Edward, 1st Lieut., Vinton, Iowa, Fort Des Moines, Iowa.
LONGO, Joseph Alfred, 1st Lieut., Omaha, Fort Des Moines, Iowa.
MacLEOD, Sherburne, 1st Lieut., Wichita, Kan., Fort Snelling, Minn.
MACAULEY, Bernard Joseph, 1st Lieut., Poplar Bluff, Mo., Fort Snelling, Minn.
NASH, Louis Rogers, 1st Lieut., Ingleside, Neb., Fort Snelling, Minn.
ORLIK, Theodore Charles, 1st Lieut., Chamberlain, S. D., Carlisle Barracks, Pa.
SALLADAY, Isaiah Reed, 1st Lieut., Pierre, S. D., Fort Snelling, Minn.
SHANE, Robert Shoemaker, Lieut. Col., Pilot Mound, Iowa, % The Governor, Des Moines, Iowa.
SPRONG, Aron Alfred, 1st Lieut., Sterling, Kan., Fort Snelling, Minn.
WESSLING, Alfred Louis, Major, Bethany, Mo., Fort Snelling, Minn.

To Carlisle Barracks

The following additional medical reserve corps officers have been ordered to extended active duty and are to report to Carlisle Barracks, Pa., for a one month refresher course and thence to permanent station, which will be designated by proper authority. This report dates from November 23 through November 29.

AKER, Grover Cecil, 1st Lieut., St. Louis.
BENINCASA, Anthony Vincent, 1st Lieut., St. Louis.
BLANKENSHIP, George William, 1st Lieut., Boonville, Mo.
COUGHLIN, Samuel Thomas, 1st Lieut., Larned, Kan.
DEVEREUX, James Aloysius, Captain, St. Louis.
DREY, Norman Walter, 1st Lieut., St. Louis.
FOWLER, Hollace Donald, 1st Lieut., Little Rock, Ark.
GUCCIONE, Joseph, 1st Lieut., St. Louis.
HAGAN, Francis James, 1st Lieut., Wichita, Kan.
HAGEN, Wayne Sigvart, Captain, Minneapolis.
HARMS, Albert Charles, 1st Lieut., Oregon, Mo.
HERMAN, Allen Isadore, 1st Lieut., Springfield, Mo.
HIRST, Ottis Grady, Captain, Prescott, Ark.
JOHNSON, John Woodrow, 1st Lieut., Kerkhoven, Minn.
LITTMANN, Lewis Ezekiel, 1st Lieut., St. Louis.
MARX, Paul Donald, 1st Lieut., Lincoln, Neb.
McMILLAN, Orin Perry, 1st Lieut., El Dorado, Ark.
MOSS, Paul, 1st Lieut., Kansas City, Mo.
ODESSKY, Louis, 1st Lieut., St. Paul.
PALMER, Henry Preston, 1st Lieut., Scott City, Kan.
POTEK, David, 1st Lieut., International Falls, Minn.
RITCHIE, Elmer Joseph, 1st Lieut., North Little Rock, Ark.
SCANLAN, Jerome Edward, 1st Lieut., St. Paul.
SCHULTE, Gregory Adrian, 1st Lieut., Joplin, Mo.
WILLIAMS, Mark Frederic, 1st Lieut., Linton, N. D.

Ordered to Fort Snelling

GLEASON, Wallace Anselm, Captain, St. Paul.

NINTH CORPS AREA

The following additional medical reserve corps officers had been ordered to extended active duty by the Commanding General, Ninth Corps Area, up to December 7. The Ninth Corps Area comprises the states of Washington, Montana, Oregon, Nevada, Utah, California and Idaho.

ALNE, Arthur E., 1st Lieut., Fullerton, Calif., Presidio of Monterey and Fort Ord, Calif.
BAER, Irving N., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
BARNARD, James F., 1st Lieut., Arlington, Calif., Presidio of Monterey and Fort Ord, Calif.
BIDWELL, Robert R., 1st. Lieut., Santa Monica, Calif., Presidio of Monterey and Fort Ord, Calif.
CLEAVE, David C., 1st Lieut., Belvedere, Marin County, Calif., Presidio of Monterey and Fort Ord, Calif.
COLLINS, Robert F., 1st Lieut., North Hollywood, Calif., Presidio of Monterey and Fort Ord, Calif.
GENDEL, Samuel, 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
GOODWIN, Ralph A., 1st Lieut., Emmett, Ida., 3d Medical Batallion, Fort Lewis, Wash.
HARRISON, Alexander V., 1st Lieut., Los Angeles, Fort MacArthur, Calif. (not Fort Lewis, as stated in THE JOURNAL, December 7).
HEATH, Richard S., 1st Lieut., Inglewood, Calif., Presidio of Monterey and Fort Ord, Calif.
HORNER, Jack C., 1st Lieut., Los Angeles, Presidio of Monterey, Calif.
HUSSER, George D., 1st Lieut., Richmond, Calif., Presidio of San Francisco.
KLOSS, Richard G., 1st Lieut., Oakland, Calif., Presidio of Monterey, Calif.
LAMB, Phillip V., 1st Lieut., Angels Camp, Calif., Presidio of Monterey and Fort Ord, Calif.
PASMORE, John L., Captain, Imola, Calif., Presidio of Monterey and Fort Ord, Calif.
POYAS, John L., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
ROSENBERG, Ralph, Captain, San Francisco, Fort MacArthur, Calif.
ROSSI, George J., 1st Lieut., San Francisco, Presidio of San Francisco.
SHEAR, Sidney P., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
SHERERTZ, Richard C., 1st Lieut., Modesto, Calif., Presidio of Monterey and Fort Ord, Calif.
TEALL, Ralph C., 1st Lieut., Sacramento, Calif., McClellan Field, Calif.

Relieved

ABRAMOPOULOS, Christos A., Major, reported ordered to extended active duty on report of week ended Nov. 8, 1940, relieved from active duty Nov. 27, 1940.

ORGANIZATION SECTION

OFFICIAL NOTES

RADIO BROADCASTS

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs being presented by the American Medical Association and the National Broadcasting Company.

The series opened Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the A. M. A. meeting at Cleveland on June 3, 1941. The program is scheduled for 10:30 p. m. eastern standard time (9:30 central, 8:30 mountain, 7:30 Pacific time) over the Blue network, other N. B. C. stations and Canadian stations.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations, and no revenue is derived from the programs. Therefore, local stations may or may not take the programs, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

Some radio stations may be unable to broadcast the program at the regular scheduled time and may transcribe and broadcast it at another hour or even on another day. It is advisable therefore to verify the time by reference to local newspapers or by telephoning the local Blue network stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in THE JOURNAL and monthly in *Hygeia*, The Health Magazine.

Tickets are available for each broadcast. Address the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Tickets are free, but a stamped self-addressed envelop should accompany requests.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

December 25. The Country Doctor.
January 1.* Otorhinolaryngologist.
January 8. Your Eyes.

* This program only will be broadcast one hour earlier than the regular scheduled time in order to clear the network for international broadcasts later in the evening.

MEDICAL ECONOMIC ABSTRACTS

MEDICAL CARE FOR MIGRATORY LABOR

The Interdepartmental Committee to Coordinate Social and Welfare Activities has recommended extension of medical care for migratory workers in the report published in the "Social Security Bulletin," September 1940, pages 3 to 15. After describing the work done in California under the Farm Security Administration, the report says:

> The committee believes that federal funds should be made available through state and local agencies to assist the states in providing health and medical services for migrants. It recommends, specifically, that the federal funds made available under titles V and VI of the Social Security Act for the fiscal year ending June 30, 1941, be augmented by the sums of $1 million and $3 million, respectively, for the purpose of initiating a program to provide essential medical care to needy interstate migrants.
>
> The committee also believes the successful administration of such a program demands that—
>
> 1. The state should participate financially in the program.
> 2. The program should provide both preventive and therapeutic services.
> 3. Federal funds should be available to all the states in accordance with the need for such grants.
> 4. The program should be applicable to all occupational groups of interstate migratory laborers.
> 5. Federal aid should be conditioned on provision for administration by a state agency and on states meeting within three years specified federal requirements covering length of residence within the state.
> 6. Social investigation, health protection and medical relief for migrants should be provided by the local agencies providing similar services for residents where such agencies exist.

AMOUNT AND TYPES OF MEDICAL CARE

The United States Public Health Service has been giving further analysis to the survey of sickness and medical care first conducted by the Committee on the Costs of Medical Care for 8,758 white families, including a total of 39,185 individuals resident "in 130 localities in 18 states representing all geographic sections."[1] The latest study of these figures is to determine the amount and type of medical care received by these persons. The total attended cases during the year that these families were kept under observation amounted to 2.9 calls per person. The total calls for those actually attended was 4.6 per case. Eighty-one per cent were attended by private general practitioners, who made 72 per cent of all calls by any type of attendant. These figures are significant in view of the challenge frequently made of the statement that between 80 and 85 per cent of all illnesses can be adequately cared for by a general practitioner. Twelve and five-tenths per cent of all cases were attended by a specialist. Private group clinics attended only 1 per cent of the cases. Three and three-tenths per cent of the illnesses were attended by nonmedical practitioners including osteopaths, chiropractors, Christian scientists and other faith healers, naturopaths, midwives and chiropodists but not dentists.

Patients are classified according to age and sex, and when the diseases characteristic of a single case are excluded the percentage of home calls was about the same for all cases.

As might have been expected, the rate of calls per thousand of population was higher in cities of 100,000 population or more than in smaller cities and rural districts. The same percentage of difference as to population was found for nonmedical practitioners.

A somewhat striking difference is found between geographic sections in respect to calls by nonmedical practitioners. Patients in the South gave the least patronage to nonmedical practitioners and California the highest, the ratio being 75 to 451. California patronage of nonmedical practitioners was more than twice as great as that of any other section of the country.

The distribution of doctors' case and call loads according to diagnosis is given in considerable detail and should be of value in calculating the probable cost of any prepayment plan for medical care. In practically all cases the greatest amount of care was required by minor respiratory disease and the second highest usually by accidents. When the cases attended by other practitioners are analyzed quite a different picture is seen. While minor respiratory is still the leading disease treated by osteopaths with rheumatic diseases second, the chiro-

1. Collins, S. D.: Frequency and Volume of Doctors' Calls Among Males and Females in 9,000 Families, Based on Nationwide Periodic Canvasses, 1828-1931, Pub. Health Rep. 55:1977 (Nov. 1) 1940.

practor reverses this order. "Backaches and other ailments" occupy the third place with both, while "nervous" receives much more attention by these types of practitioners than by physicians. When it comes to the number of calls, rheumatic diseases lead in the practice of both osteopaths and chiropractors, making up 13.6 and 14.1 per cent of their entire practice, while they require but 3.2 per cent of the care given by general practitioners. The report of the Public Health Service comments on this feature as follows:

> The lack of definite diagnoses for illnesses treated only by nonmedical practitioners tends to increase the number of ill defined cases; in spite of this tendency the picture seems reasonably true, namely that it is the various rheumatic and other indefinite chronic pains that bring the patient to a nonmedical practitioner. Aside from this, sprains and other cases where massage therapy is commonly applied also fall into the hands of such practitioners.

WOMAN'S AUXILIARY

Delaware

The annual meeting of the auxiliary to the Delaware Medical Society met in Rehoboth, October 3, with thirty-eight members present.

Weekly meetings for Red Cross work were voted on. A committee was appointed to collect clothes for the British War Relief.

Dr. A. R. Shands, the guest speaker, spoke on the recently opened Nemours foundation, a hospital for crippled children of Delaware.

Iowa

At the executive board meeting of the woman's auxiliary to the Iowa State Medical Society in Des Moines, September 16, Mrs. V. E. Holcombe, national president, addressed the group on the increasing influence and responsibility of women. Also present were Dr. James C. Hill and Dr. John G. de Bey, members of the advisory council. Each addressed the group, giving valuable suggestions regarding the role of the doctor's wife as an individual and the auxiliary as a unit in promoting medical interests.

A recent addition to the state organization was reported as the Upper Des Moines Auxiliary, comprising the counties of Emmet, Dickinson, Clay and Palo Alto.

Nebraska

The auxiliary to the Lancaster County Medical Society met October 7. The speaker was Prof. O. H. Bimson of Lincoln High School, who talked on his experiences as a member of the Educational Policies Commission and the American Youth Commission.

The Omaha-Douglas county medical auxiliary held a Harvest Home Benefit Dinner October 9. Proceeds from the dinner will benefit the projects adopted at the recent membership tea: namely subscriptions to *Hygeia* to all 102 of Omaha's public and parochial schools and contributions to the Community Chest, the School Free Lunch Fund and the Nebraska Tuberculosis Health Camp.

A joint meeting of the tri-county auxiliary No. 1 and the Tri-County Medical Society was held recently at the St. Francis Hospital in Grand Island. The nurses' glee club sang during the dinner hour. At the auxiliary meeting after reports were given by committee chairmen Mrs. Elmer Hansen spoke on auxiliary problems; Mrs. J. G. Woodin, president of the auxiliary, gave a talk on "A Look Ahead," and Mrs. A. D. Broun, state president, addressed the group.

The Woman's Auxiliary to the Adams County Medical Society met at Ingleside. Mrs. L. W. Rork presided. There was a business meeting preceded by a musical program given by the occupational therapy department at Ingleside.

New York

The Woman's Auxiliary to the Albany County Medical Society entertained, September 17, the wives of members of the third district branch to the state medical society, which includes Schoharie, Albany, Rensselaer, Greene, Columbia, Sullivan and Ulster counties. The auxiliaries of Columbia County and of Albany County held their regular meeting at this time and invited doctors' wives of unorganized counties. October 23, the Albany auxiliary was addressed by Dr. Louis Bauer, a member of the medical preparedness committee of the New York State Medical Society.

At the annual dinner of the auxiliary to the Cayuga County Medical Society the sum allotted for the dinner was presented to the American Red Cross. Mrs. G. B. Adams, president-elect of the woman's auxiliary to the state society, was guest of honor at a tea to which members of the Onondaga County auxiliary were present.

The auxiliary to the Essex County Medical Society was organized, June 4, at the semiannual meeting of the society. Mrs. G. Scott Toune, past state president, Mrs. T. C. Bullard of Saratoga and Mrs. R. F. Johnson of Cayuga gave talks. With the organization of the Essex County auxiliary there are twenty-four counties organized in New York State.

The first meeting of the year in Nassau County was a membership tea, September 24. Guests were greeted by the president of the auxiliary, Mrs. A. C. Martin, and by Dr. Aaron Higgins, president of the county medical society.

The fourth district branch of the state medical society held its annual meeting in Schenectady October 1 and 2. The wives of all the doctors in the district were entertained by the auxiliary. The presidents of counties having auxiliaries acted as hostesses for the day and the wives of the presidents of the unorganized counties and wives of the officers of the district branch were guests of honor.

Ohio

A meeting of the executive board of the Woman's Auxiliary to the Ohio State Medical Association was held in Columbus, October 9, with Mrs. J. Edwin Purdy, the president, presiding. She expressed appreciation that all the members were present and then introduced Mrs. V. E. Holcombe, the national president. Mrs. W. H. Curtiss, Chairman of Organization, reported that about forty counties had organized. The meeting adjourned, to meet in Cleveland in June.

Utah

The auxiliary to the Weber County Medical Society held its first meeting of the year on Monday, October 7, at the home of Mrs. Joseph R. Morrell in Ogden. "Health Insurance" was discussed by Dr. G. M. Fister, and there was music by Mrs. O. S. Daines. Mrs. A. Z. Tanner, Layton, the new president, was in charge.

The Salt Lake County medical auxiliary held a meeting at the Hotel Utah Roof Garden. The first speaker was Dr. E. M. Neher, advisory chairman. The new officers were introduced, and Mrs. John Z. Brown gave some history of the Salt Lake County organization. She introduced those who were present who had served as presidents. Dr. Dee L. Folsom of the Salt Lake Dental Society spoke in the interests of impending legislation of interest to both dentists and doctors in Utah and Salt Lake City.

Wisconsin

The Woman's Auxiliary to the Douglas County Medical Society, with Mrs. E. A. Myers presiding, met October 7 in Superior. Miss Aimee Zillmer of the state health department spoke on "Social Hygiene." For a special project Miss Zillmer was kept in the county for two weeks, being presented to twelve different civic organizations, including all of the P. T. A. groups in the city of Superior, all of the junior and senior high schools in the city and county, the Teacher's College and some special classes in the college.

Red Cross work was started in November by the Manitowoc County auxiliary, of which Mrs. Theodore Tietgen of Manitowoc is president.

The Washington-Ozaukee auxiliary is taking up Red Cross work. At the October 10 meeting two members volunteered to knit and twelve to sew. Mrs. A. H. Heidner of West Bend is the new president.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS AND ARTICLES APPEAR IN THE STUDENT SECTION, PAGE 2227.

CALIFORNIA

Surgical Meeting.—The Los Angeles Surgical Society held its annual meeting, December 13, with Dr. Rolland Russell Best, associate professor of surgery, University of Nebraska College of Medicine, Omaha, as the guest speaker. His subject was "Indications for the Biliary Flush." Others on the program included:

Dr. George Lawrence Chaffin, Ruptured Diverticulitis of the Colon.
Dr. Emmet A. Pearson, Heterotopic Endometriosis.
Dr. Charles W. Reeder, Long Beach, Idiopathic Segmental Infarction of the Greater Omentum.
Dr. William H. Snyder Jr., Extensive Carbuncle of the Neck.
Dr. Arthur E. Smith, Bilateral Condylectomy in a Patient with Multiple Fractures of the Mandible.

Breakfast Club Organized.—Forty-five members of the staff of the Methodist Hospital of Southern California, Los Angeles, have organized a breakfast club which meets at the hospital on the first and third Wednesday morning of the month. Each meeting starts at 7:30 a. m. and ends promptly at 9. Chairmanship of each meeting is chosen by lot. Two cases are presented which have been previously abstracted from actual case reports. Copies are distributed for perusal during breakfast. The names of patient and physician are withheld to stimulate informality and freedom of discussion. A name is drawn from those present and this physician may ask any questions to work up the case. He gives the diagnosis and outlines the treatment that he would follow. This is compared with the chart diagnosis and treatment and general discussion follows. Each of these two cases takes twenty-five minutes, after which a short prepared paper of interest to all is given by one of the members.

ILLINOIS

Conference on Public Health.—The Illinois Conference on Public Health was held in Springfield, December 5-6. Among the speakers were:

Dr. Halbert L. Dunn, Washington, D. C., Using Vital Statistics as a Program Guide.
Howard J. Shaughnessy, Ph.D., Chicago, Milk-Borne Disease.
Dr. Robert S. Breakey, Lansing, Mich., Sex Education in High Schools.
Dr. Harry S. Mustard, New York, Public Health in National Defense.
Dr. Richard E. Shope, Princeton, N. J., Epidemiology of Virus Diseases.
Dr. Donald K. Hibbs, Chicago, Chemotherapy in the Treatment and Control of Gonorrhea.

Chicago

Activities of Tumor Institute.—The Chicago Tumor Institute has issued a report of its activities for its first two years. Of 904 patients observed, 613 patients had cancerous lesions, while 301 had benign tumors, inflammatory lesions and other noncancerous conditions. It is of special significance, says the report, that of the 613 cancer patients 262, or 42.7 per cent, had far advanced cancers, and it is sad to reflect that the greater number were cases of accessible forms of cancer easily curable in early stages. Of the total number of patients, 622 were residents of Chicago, 140 came from cities in Illinois outside of Chicago, 130 from twenty-four other states and 12 from six foreign countries. Procedures carried out included 13,269 examinations, 8,846 roentgen diagnoses, 7,756 roentgen treatments, 4,432 radium treatments, 184 minor surgical procedures, seventy-eight surgical procedures, and the making of 278 photographs and lantern slides. An attempt is being made to pursue a five year follow-up of all cancer patients treated at the institute and in the group of 904 observed only 1 patient remained untraced at the end of the first two years. Every patient who was treated has been traced. "Cancerphobia" is attributed to 34 patients of the 904 who came to the institute because of fear they were suffering from cancer. The disease was not found in any of this group. Seventeen, or 50 per cent, are classified as having general phobias, and of the remainder one third referred their complaints to the breast, one third to the mouth and one third to the gastrointestinal and genitourinary systems. In the first two years, two courses have been held and instruction has been given to forty-nine qualified radiologists, thirty-six from the United States and thirteen from foreign countries. Eighty physicians from thirty foreign countries visited the institute to study its organization and equipment and consult with the staff on various phases of the cancer problem. The institute was opened in March 1938 and the report covers the period ended March 31, 1940.

INDIANA

Chief of Local Health Administration.—Dr. George M. Brother, Rising Sun, formerly director of district health unit number 4, has been appointed chief of the bureau of local health administration of the state board of health. He succeeds Dr. John W. Ferree, Indianapolis, who recently became director of the board of health. Dr. Brother recently took a degree in public health at Johns Hopkins University School of Hygiene and Public Health, Baltimore. He graduated at Indiana University School of Medicine, Indianapolis, in 1934.

IOWA

Aid for Research.—Grants-in-aid for research have been received recently by the following staff members of the State University of Iowa College of Medicine, Iowa City: Harry M. Hines, Ph.D., of the department of physiology, $5,000 from the National Foundation for Infantile Paralysis for study of regeneration of nerve and muscle; Dr. William D. Paul of the department of theory and practice, $3,500 from the Emerson Drug Company for the study of the action of bromides, and Dr. Philip C. Jeans of the department of pediatrics, $3,000 from the Mead Johnson Company for a continuation of studies on infant nutrition.

KANSAS

Society News.—Dr. Willis H. McKean, Kansas City, addressed the Wyandotte County Medical Society, November 19, on "Surgical Treatment of Empyema" and Dr. Maurice A. Walker, Kansas City, "Minor Surgery in the Office."——Drs. Fred J. McEwen and James B. Fisher addressed the Sedgwick County Medical Society in Wichita, November 19, on "Pulmonary Embolism" and William P. Callahan, "Medical Preparedness." Drs. Rolland Russell Best and Frank Lowell Dunn, both of Omaha, presented the program before the society, November 6; their subjects were, respectively, "Biliary Flush as an Aid in Surgery and Medical Treatment of Biliary Tract Diseases" and "Modern Undernutrition."

LOUISIANA

Changes in Health Officers.—Dr. William C. Summer, Minden, director of the Webster Parish health unit for the past ten years, has resigned to become consultant adviser to the parish health units in eighteen parishes of northern Louisiana. He will be succeeded by Dr. Edmond G. Klamke, New Roads, health director of Pointe Coupee Parish.——Dr. John M. Whitney, Jennings, head of the Jefferson Davis Parish health unit, has been made director of fifteen parish health units in southwestern Louisiana; the area runs from the Texas line to Terrebonne Parish on the south to Pointe Coupee Parish on the north.

Refresher Course.—A refresher course in obstetrics will be conducted at the Louisiana State University Medical Center, January 6-18. The group is limited to eight physicians, so that each may receive individual attention. Additional courses will be offered later in the year. The course is being financed by social security funds allocated to the state by the Children's Bureau, U. S. Department of Labor. Applications of physicians interested in taking the course should be sent to the Maternal and Child Health Division, 313 Civil Courts Building, New Orleans, on or before December 1. Applications will be reviewed by a committee from the state medical society, who will select the physicians to take the course.

NEW JERSEY

District Meeting.—Dr. Frank H. Lahey, Boston, President-Elect of the American Medical Association, addressed a meeting of the Fifth Councilor District of the Medical Society of New Jersey, December 19, in Woodbury, on "Management of Diseases of the Thyroid." The Gloucester County Medical Society was host.

Special Society Meeting.—Dr. Hyman I. Goldstein, Camden, was elected president of the New Jersey Gastroenterological Society at its annual meeting in Newark, December 2. Dr. Harrison R. Wesson, Montclair, was elected vice president and Dr. Sydney Rosenthal, Newark, secretary. A public meeting will be held by this society February 3, at which a symposium on "Ulcer of the Stomach and Duodenum" will be presented.

NEW YORK

The State Society's Postgraduate Courses.—The council committee on public health and education of the Medical Society of the State of New York has arranged several courses for county societies. A course on general medicine is being presented before the Schoharie County Medical Society on Tuesday afternoons at Cobleskill and the Montgomery County society Tuesday evenings at Amsterdam with the following speakers:

November 19, Dr. David D. Moore, New York, Diabetes Mellitus.
November 26, Dr. Kenneth R. McAlpin, Williamstown, Mass., A General Consideration of Anemia, Both Primary and Secondary.
December 3, Dr. Harold J. Stewart, New York, Digitalis Therapy: Mechanism of Its Action in Congestive Heart Failure.
December 10, Dr. Albert Vander Veer, New York, Asthma.
December 17, Dr. Leslie P. Barker, New York, Syphilis.
January 7, Dr. Homer F. Swift, New York, Rheumatic Fever.
January 14, Dr. John D. Lyttle, New York, Nephritis.

Two courses are in progress for the Nassau County Medical Society. One on pediatrics, arranged in cooperation with the state department of health, has the following schedule:

November 25, Dr. Charles Hendee Smith, New York, Diet of Infants and Children.
December 23, Dr. Hugh Chaplin, New York, Care and Feeding of Prematures.
January 27, Dr. Gaylord W. Graves, New York, Preventive Pediatrics and the Periodic Health Examination.
February 24, Dr. Philip M. Stimson, New York, The Infectious Diseases.
March 24, Dr. Frederick H. Wilke, New York, The Anemias of Childhood.
April 28, Dr. Katharine G. Dodge, New York, Rheumatic Fever, Chorea and Heart Disease.

The following speakers are announced for a course in general medicine in Nassau County:

November 18, Dr. Ralph G. Stillman, New York, The Significance of Laboratory Tests and Methods in the Practice of Medicine.
December 16, Dr. Harry H. Gordon, New York, Endocrine Problems in Adolescence.
January 20, Dr. Norman H. Plummer, New York, Newer Chemotherapeutic Methods.
February 17, Dr. Norman H. Jolliffe, New York, The Relation of Vitamins to Disease.
March 17, Dr. Edward M. Livingston, New York, Abdominal Pain.

New York City

Public Lectures.—The New York Academy of Medicine opened its sixth annual series of "Lectures to the Laity," November 14, with the Linsly R. Williams Memorial Lecture, by Dr. Alan Gregg, on "Humanism and Science." Others in the series are as follows:

Dr. William Healy, Boston, Psychiatry and the Normal Life, December 12.
Dr. Henry E. Sigerist, Baltimore, Paracelsus in the Light of Four Hundred Years, January 23.
Dr. Francis Carter Wood, New York, What We Do Know About Cancer, February 27.
Irwin Edman, Ph.D., New York, Philosophy as Therapy, March 27.
Oscar Riddle, Ph.D., Cold Spring Harbor, The Promise of Endocrinology, April 24.

Dr. Meleney Comes to New York University.—Dr. Henry E. Meleney, associate professor of preventive medicine and public health at Vanderbilt University School of Medicine, Nashville, Tenn., has been appointed Hermann M. Biggs professor of preventive medicine at New York University College of Medicine, effective April 1, 1941. Other appointments announced are:

Dr. Conrad Berens, associate professor of ophthalmology.
Dr. Wendell L. Hughes, clinical professor of ophthalmology.
Dr. Charles W. Lester, assistant clinical professor of surgery.

Dr. Robert F. Pitts, instructor in physiology, has been promoted to assistant professor of physiology.

Dr. Mustard Honored.—The Alumni Association of the De Lamar Institute of Public Health, Columbia University College of Physicians and Surgeons, gave a dinner, November 19, at the Hotel George Washington in honor of Dr. Harry Stoll Mustard, director of the institute. Leonard J. Ciccoli, Ph.D., president of the association, presided, and the speakers were Drs. Mustard; Wilson G. Smillie, professor of public health and preventive medicine, Cornell University Medical College, and Comdr. Charles S. Stephenson, an alumnus, in charge of the division of preventive medicine, Bureau of Medicine and Surgery, U. S. Navy. Dr. Mustard was appointed last April to succeed Dr. Haven Emerson as director of the institute.

NORTH CAROLINA

Anniversary at Duke University.—The tenth anniversary of Duke University School of Medicine and Duke Hospital, Durham, was observed, November 29-30. An addition to the hospital and a new department of psychiatry were dedicated. Dr. Adolf Meyer, Henry Phipps professor of psychiatry of the Johns Hopkins University School of Medicine, Baltimore, conducted a clinic to mark the opening of the new psychiatric wards, which are named in his honor. The wards provide eighteen beds for the use of the new department. Dr. Richard S. Lyman, formerly of Baltimore, has been appointed professor of psychiatry. The new hospital wing is five stories high and has two hundred rooms providing one hundred and thirteen additional beds and eighty new offices and examining rooms. At the ceremony Dr. Frederic M. Hanes, Florence McAlister professor of medicine, presided. The speakers were Robert L. Flowers, acting president of the university, and Dr. Wilburt C. Davison, dean of the school of medicine. Another feature of the two day program was a clinic at which Dr. Jay M. Arena presided, and addresses were made by Drs. Hanes, David T. Smith, Julian Deryl Hart and Francis Bayard Carter. At a dinner, Friday, at the University Union, the alumni association was formally organized, with Drs. Arena as president; Robert W. Graves, vice president, and J. Lamar Callaway, secretary. All are on the Duke Hospital staff. Duke Hospital received its first patient July 21, 1930, and has since received more than 143,000 patients. The school of medicine opened in October 1930 and has graduated 374 physicians.

OHIO

The Lower Lecture.—Edward A. Doisy, Ph.D., professor of biochemistry, St. Louis University School of Medicine, delivered the third annual Lower Lecture of the Academy of Medicine of Cleveland, November 15. His subject was "Vitamin K and Other Antihemorrhagic Compounds."

Personal.—Dr. Torald H. Sollmann, dean and professor of pharmacology and materia medica, Western Reserve University School of Medicine, Cleveland, received the "degree of merit" of Nu Sigma Nu at the annual convention of the fraternity in Detroit, November 23.——Dr. James C. Elder, Millersburg, has resigned as health officer of Holmes County.

Society News.—Dr. John Scudder, New York, addressed the Academy of Medicine of Cincinnati, November 19, on "Shock: Blood Studies as a Guide to Therapy."——Dr. Edward H. Rynearson, Rochester, Minn., addressed the Stark County Medical Society, Canton, November 14, on "Diabetes Mellitus and Hyperinsulinism."——A symposium on "Low Back Pain" was presented at a meeting of the Columbus Academy of Medicine, November 18, by Drs. Judson D. Wilson on "Injury to Articular Facets"; Roy J. Secrest, "Herniated Intervertebral Disk," and Harry E. Le Fever, "Hypertrophied Ligamentum Flavum."——Dr. Robert R. Crawford, Mansfield, addressed the Ashland County Medical Society, Ashland, November 15, on the care of fractures.——Dr. Harold Feil, Cleveland, discussed "Cardiac Emergencies and Their Treatment" at a meeting of the Lorain County Medical Society, Elyria, November 12.——Dr. Carlo J. Tripoli, New Orleans, addressed the Montgomery County Medical Society, Dayton, November 15, on "New Developments in the Treatment of Meningitis."

PENNSYLVANIA

Society News.—Dr. Newlin F. Paxson, Philadelphia, addressed the Delaware County Medical Society, Chester, November 14, on "Chronic Nephritis and Pregnancy."——Dr. George P. Müller, Philadelphia, addressed the Cambria County Medical Society, Johnstown, November 14, on "Cancer of the Stomach."——The Lycoming County Medical Society held an all day meeting in Williamsport, November 8, with the following speakers: Drs. Leonard G. Rowntree, Philadelphia, on cardiovascular disease; Lewis C. Scheffey, Philadelphia, gynecology; Harrison F. Flippin, Philadelphia, and Dale C. Stahle, Harrisburg, a symposium on pneumonia.——The annual William Moore Guilford Memorial Clinic was presented by the Lebanon County Medical Society, Lebanon, November 26. Dr. Baldwin H. E. W. Lucke, Philadelphia, conducted the clinic on "Edema of Renal Origin."——Dr. Marshall M. Lieber, Philadelphia, addressed the Washington County Medical Society, Washington, November 6, on "Newer Concepts on the Mechanism of Inflammation and Shock—Some Practical Considerations."

GENERAL

Outbreaks of Influenza.—An extensive outbreak of an apparently mild type of influenza was reported December 16 in Alexandria, La. This city has recently nearly doubled its normal population of 30,000 owing to the influx of army camp workers and others who have flocked there in view of the military training program at Camp Beauregard nearby. Several thousand cases of influenza are said to have developed chiefly among the camp construction workers and others, many of whom were living under unsatisfactory housing conditions. No cases were reported among the soldiers at Camp Beauregard. The Chicago *Tribune* reports that the influenza epidemic in the Western states, now waning in California, has spread to Washington and Oregon. Schools were closed in Bellingham, Wash., December 13 and in Portland December 16. Influenza has also been reported in Texas and Kentucky.

Grants for Research in Endocrinology.—Requests to the National Research Council Committee for Research in Endocrinology for aid during the fiscal period from July 1, 1941 to June 30, 1942 will be received until Jan. 31, 1941. Application blanks may be obtained by addressing the Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington, D. C. In addition to a statement of the problem and research plan or program, the committee wants information on the proposed method of attack, the institutional support of the investigation and the uses to be made of the sum requested. No part of any grant may be used by the recipient institution for administrative expenses. Applications for aid of endocrine research on problems of sex in the narrower sense cannot be given favorable consideration, but the committee will consider support of studies on the effects of sex hormones on nonsexual functions, for example on metabolism.

Fund Available for Research.—The next meeting of the American Academy of Arts and Sciences to consider applications for assistance in scientific research will be held February 15. Income from the Permanent Science Fund, according to agreement and declaration of trust, shall be applied by the academy to such scientific research as shall be selected ". . . in such sciences as mathematics, physics, chemistry, astronomy, geology and geography, zoology, botany, anthropology, psychology, sociology and economics, history and philology, engineering, medicine and surgery, agriculture, manufacturing and commerce, education and any other science of any nature or description, whether or not now known or now recognized as scientific, and may be applied to or through public or private associations, societies, or institutions, whether incorporated or not, or through one or more individuals." Additional information may be obtained from the chairman of the Committee on the Permanent Science Fund, Prof. John W. M. Bunker, Massachusetts Institute of Technology, Cambridge, Mass.

Psychiatric Association Plans Public Education Program.—The committee on public education of the American Psychiatric Association announces the appointment of twelve regional chairmen to cooperate with the press and otherwise "to foster the dissemination of sound psychiatric information to the public." The chairmen are Drs. Franklin G. Ebaugh, Denver; Ralph C. Hamill, Chicago; Titus H. Harris, Galveston, Texas; Richard H. Hutchings, Utica, N. Y.; George S. Johnson, San Francisco; William C. Menninger, Topeka, Kan.; Merrill Moore, Boston; Arthur P. Noyes, Norristown, Pa.; Winfred Overholser, Washington, D. C.; Thomas A. Ratliff, Cincinnati; Newdigate M. Owensby, Atlanta, Ga., and Karl M. Bowman, New York. In addition to providing the press of these regions with an authoritative source of information on psychiatric matters, the association will stress its policy with regard to mental hospital standards, it was said. "One of the principal aims of this organization will be to acquaint the public with the fact that a well staffed, well equipped hospital for the care of the mentally ill is not a luxury, but a basic necessity in any civilized community," the statement said.

Annual Forum on Allergy.—Allergists of the Middle West will hold their third annual forum to review progress in the clinical study of allergy in Indianapolis, January 11-12, at the Claypool Hotel. Methods of instruction will include study groups under different instructors, exhibits, special lectures, question and answer periods and symposiums. The annual Forum Lecture will be delivered Sunday by Dr. Béla Schick, New York, on "Allergy, Hypersensitiveness and Immunity." Dr. Schick will receive a gold medal honoring him for "distinguished and outstanding contributions in the field of allergy." The other special lectures will be delivered by Dr. Albert D. Ruedemann, Cleveland, on "Allergic Manifestations in the Eye," and by Dr. Malcolm M. Cook, St. Louis, "Water and Electrolyte Metabolism in Allergy." The symposiums will be on "Bronchial Asthma," with Dr. Ben Z. Rappaport, Chicago, as moderator; "Insects as Allergens," Dr. Harry L. Huber, Chicago, and "Allergic Headache," Dr. Theodore L. Squier, Milwaukee. All physicians in good standing in their local medical societies will be welcome. There will be a registration fee of $5. Registrations should be mailed to Dr. Tell Nelson, 636 Church Street, Evanston, Ill.

Special Society Elections.—Dr. John H. Moore, Grand Forks, N. D., was chosen president-elect of the Central Association of Obstetricians and Gynecologists at its recent annual session in Indianapolis and Dr. Thomas B. Sellers, New Orleans, was installed as president. Other officers include Drs. Minnie L. Maffett, Dallas, vice president, and William F. Mengert, Iowa City, secretary-treasurer. New Orleans was selected as the place of the 1941 meeting, the exact date to be announced later.——Dr. Bruce H. Douglas, Detroit, was elected president of the Mississippi Valley Conference on Tuberculosis at the annual meeting in St. Paul, October 2-4. Donald E. Pratt, executive secretary of the Missouri Tuberculosis Association, was elected vice president, and A. W. Jones, executive secretary of the St. Louis Tuberculosis and Health Society, was reelected secretary. Dr. George C. Turner, Chicago, was elected president of the Mississippi Valley Sanatorium Association, which met in conjunction with the tuberculosis conference. Dr. Francis F. Callahan, Pokegama, Minn., was elected vice president and Dr. Henry S. K. Willis, Northville, Mich., secretary.——Dr. Marcus Pinson Neal, Columbia, Mo., was chosen president-elect of the Southern Medical Association at the annual meeting in Louisville, Ky., November 12-15. Dr. Paul H. Ringer, Asheville, N. C., was elected president, taking the place of Dr. Quitman U. Newell, St. Louis, the president-elect, who died a few days before the meeting. Drs. Ernest Lee Heflin, Louisville, and James R. Bloss, Huntington, W. Va., were elected vice presidents. Next year's meeting will be in St. Louis.——Ernest Carroll Faust, Ph.D., New Orleans, was chosen president-elect of the American Society of Tropical Medicine at its annual meeting in Louisville, Ky., November 12-15, in conjunction with the Southern Medical Association. Dr. Thomas T. Mackie, New York, was installed as president; Dr. Fred L. Soper, Rio de Janeiro, Brazil, was made vice president, and Dr. E. Harold Hinman, Wilson Dam, Ala., secretary.——Dr. Earl E. Kleinschmidt, Chicago, was chosen president-elect of the American School Health Association at its recent annual meeting and Dr. Amos L. Beaghler, Denver, was inducted into the presidency. Dr. Helen Irene Ahrens Cary, Portland, Ore., and Lon W. Morrey, D.D.S., Chicago, were chosen vice presidents. Dr. Arville O. DeWeese, Kent, Ohio, is the executive secretary-treasurer.——Gobind Behari Lal, New York, science editor of International News Service and the Hearst newspapers, was elected president of the National Association of Science Writers at its annual meeting. Robert D. Potter, science editor of the *American Weekly*, New York, is vice president; Miss Jane Stafford, medical writer, Science Service, Washington, D. C., secretary, and Stephen J. McDonough, science writer, Associated Press, Washington, treasurer.

Government Services

The Government Needs Technicians

The U. S. Civil Service Commission requests applications for positions as senior medical technician at $2,000 a year, medical technician at $1,800, and assistant medical technician at $1,620. The senior technician may offer general subjects or specialize in roentgenology; the medical technician and the assistant may have their choice of surgery, roentgenology or general subjects. This announcement is an amendment of an earlier one which did not include "general" in the optional subjects. Applications must be on file with the commission at Washington, D. C., not later than December 30 if from states other than the following: Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming. For the Western states the deadline is January 2.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 13, 1940.

The Chemotherapy of War Wounds

At the Medical Society of London a discussion took place on chemotherapy in war wounds. Col. Max Page said that it was not until 1939 that surgeons took any interest in the use of sulfonamide derivatives in the treatment of wound infection. Experimental work, mainly on mice, indicated that they had a prophylactic value. Plans were made for trying them in the war, but the nature of the campaign in France and Flanders allowed only sporadic attempts as far as recorded evidence went. His own impression was that the incidence of secondary infection in wounds treated with sulfanilamide was lower than might have been expected from the last war. The condition in which prophylactic use of a sulfonamide was probably good was a late wound, twenty-four or thirty-eight hours or perhaps a week after infection, requiring operation and suggesting the possibility of a flare-up. If a full dose was given by mouth beforehand, intervention would be safer. In treatment a few doses would on most occasions deal with an acute streptococcic infection but not with a chronic infection. When the infection was in the blood the drug was not of the same value as when it was in the body tissues. The same held for gas gangrene.

Colonel Colebrooke said that definite results were to be expected from careful use of sulfonamide derivatives. The first was the prevention of hemolytic streptococcus infection. But the great majority of the wounded in war were not infected with hemolytic streptococci at the time of the injury. Their infection occurred at any time within a week afterward as a hospital infection. A sulfonamide derivative would be valuable in a case of secondary operation in which there was a suspicion of hemolytic streptococcus infection. Prophylactic treatment should be administered in four hourly doses. It might also be possible to arrest infection by prompt and vigorous action. In long-standing or superficial cases, such as old burns and road accidents which had led to infection, the application of sulfanilamide powder gave astonishingly good results.

Mr. W. H. Ogilvie said that infection seemed to be a far less serious problem in this war than in the last. The explanation was not simple. The wounded were far less fatigued and dehydrated; their clothes were cleaner; many of the weapons were less damaging to the tissues than the shell and hand grenades which were so much used in the last war. He thought that the streptococci and anaerobic organisms of today were feeble compared with their ancestors of 1914-1918. But after making these allowances much credit must go to chemotherapy. In the wounded from the evacuation of Dunkirk chemoprophylaxis when started early put the patients in good condition, while those who arrived infected at the hospital in whom chemotherapy was started immediately after débridement soon showed repair and clean granulation. The contrast between the wounds of those who had been given a sulfonamide derivative in transit and those who had not was great. The latter when admitted two or three days after being wounded were most heavily infected. On being put on a sulfonamide derivative they had a temperature which rarely rose above 100 F. or remained elevated more than three or four days. Sir Thomas Dunhill referred to 65 patients treated in the hospital, all extremely ill. Their knees and elbows were shattered and ankles broken. Pus was soaking through the plaster, and the stench was beyond belief. In the last war he would have felt that that three fourths would require amputation and that streptococcic septicemia would occur. They were treated by fixation and a sulfonamide derivative for a number of days until it was felt that appropriate doses had been given. Two died from secondary hemorrhage and one from gas gangrene, but all the rest did well. He believed that three fourths of the results was due to fixation and the rest to the sulfonamide derivative. Together they seemed to be able to scotch the spread of infection.

Gas Gangrene

The War Wounds Committee of the Medical Research Council and the Committee of London Sector Pathologists have published a review of gas gangrene based on the experience of the last great war and on recent experience in Spain, France and elsewhere. As these committees are composed of leading surgeons and pathologists the pamphlet, which is published by the government, is authoritative. For prophylaxis, excision of contaminated war wounds at the earliest opportunity is recommended. But when injured men come under observation only at a later period, when organisms have already reached the living tissues bordering on the wound cavity or when the wound is passing through a stage of physiologic reaction to injury, the time for prophylactic excision has passed and the surgeon should aim at providing adequate drainage by incision. In late cases, however, in which there is any suspicion of gangrenous infection of muscle, the wound must be opened up and the muscles implicated must be ruthlessly excised.

Recent laboratory experiments indicate that the best available treatment, in addition to surgery, for the established disease is a combination of antitoxin and chemotherapy with sulfapyridine or sulfanilamide. The serum and the drug seem to have a synergic action, the former neutralizing the bacterial toxin, while the latter exercises a bacteriostatic effect on the organism. The antitoxin should be administered, preferably intravenously, at the earliest possible moment. The dose of polyvalent antitoxin recommended is 7,500 international units of Clostridium welchii, 3,750 of Clostridium septique and 2,500 of Clostridium oedematiens, repeated as necessary. The first dose of sulfapyridine or sulfanilamide should be 2 Gm. dissolved in hot citric acid or lemon solution. Subsequent doses, starting two hours later and continued four hourly for two days, should be 1 Gm. uncrushed. After the first two days the dose should be gradually reduced as the condition improves, but the interval between the doses should not be more than six hours for several days. Small doses, e. g. 3 Gm. daily, should be continued for three or four days after the temperature has become normal. The duration of treatment and the total dosage will vary somewhat, but the latter should seldom exceed 35 Gm.

In cases in which the surgeon has to operate on a wound in which anaerobic infection is already established, preoperative sulfapyridine or sulfanilamide by mouth and antitoxin intravenously may be useful in preventing the spread of infection. The first dose of the drug should be 3 Gm., which should, if possible, be given two hours before operation so as to secure a high concentration in the blood when the wound is disturbed.

Marriages

DAVID BRAINARD GREGG, Greensboro, N. C., to Miss Mary Page Newton of Charleston, S. C., October 17.

WILLIAM C. BEHEN, Lansing, Mich., to Miss Rose Lucille Megerle of Newport, Ky., October 14.

DUWARD O. WRIGHT, Fort Payne, Ala., to Miss Harriet D. Harton at Conway, Ark., October 5.

JOHN J. SCHOFF, Media, Pa., to Miss Charlotte Fullerton of Swarthmore, November 8.

DAVID ROSENBLOOM to Miss Esther Shamir, both of Los Angeles, September 21.

JOHN JIBB THORNTON to Miss Marion Faye Gager, both of Cleveland, October 11.

Deaths

Edgar Alphonso Hines ⊕ Seneca, S. C.; Medical College of the State of South Carolina, Charleston, 1891; member of the House of Delegates of the American Medical Association from 1910 to 1928 and from 1930 to 1940; vice chairman of the state board of health for many years and one of the founders of the board's bureau of child hygiene; past president of the South Carolina Pediatric Society and the Piedmont Postgraduate Clinical Assembly; member of the American Academy of Pediatrics; fellow of the American College of Physicians; in 1913, session chairman of the International Congress of School Hygiene in Buffalo; for many years trustee and chairman of the school board; on the staff of the Oconee County Hospital; superintendent of the Anderson County Hospital, Anderson, for 1915; secretary of the South Carolina Medical Association; secretary-treasurer of the Oconee County Medical Society; editor in chief of the *Journal of the South Carolina Medical Association;* chairman of the Committee on Medical Preparedness for South Carolina; aged 73; died, November 27, of coronary occlusion.

Philip King Brown ⊕ San Francisco; Harvard Medical School, Boston, 1893; assistant in nervous diseases, University of California Medical School in 1894, associate professor of clinical medicine from 1896 to 1898 and instructor of animal pathology from 1896 to 1899; associate in medicine and instructor of clinical pathology, Cooper Medical College from 1899 to 1902; member of the Association of American Physicians and the American Clinical and Climatological Association; served in various capacities and at various times on the staffs of the Southern Pacific Hospital, Stanford University Hospital and the City and County Hospital, San Francisco; secretary of the board of directors, founder and for many years medical director of the Arequipa Sanatorium, Manor; aged 71; died, October 29, of coronary thrombosis.

Lemuel Payson Adams ⊕ Oakland, Calif.; University of Vermont College of Medicine, Burlington, 1899; member of the House of Delegates of the American Medical Association in 1925; senior fellow of the Pacific Coast Surgical Association; a founder of the American Association for the Surgery of Trauma and of the American Board of Surgery; fellow of the American College of Surgeons; chief of the East surgical staff of the Alameda County Hospital, Oakland, and the Fairmount Hospital, San Leandro; a director and member of the staff of Peralta Hospital, Oakland; aged 65; died, October 27, of coronary embolism.

Jackson Thornwell Witherspoon ⊕ New York; Johns Hopkins University School of Medicine, Baltimore, 1928; member of the Indiana State Medical Association; formerly instructor and later assistant professor of gynecology at Tulane University of Louisiana School of Medicine, New Orleans, and assistant professor and subsequently associate professor of gynecology at the Indiana University School of Medicine, Indianapolis; author of "Clinical Pathological Gynecology"; at one time editor of *Modern Medicine;* aged 40; died, October 19, at his home in Darien, Conn.

John Henry Rishmiller ⊕ Gibbon, Minn.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1891; an Affiliate Fellow of the American Medical Association; fellow of the American College of Surgeons; past president of the American Association of Railway Surgeons; formerly chief surgeon of the Soo Line; at one time on the staff of the City Hospital and Swedish Hospital, Minneapolis; aged 74; died, October 15, of cerebral embolism, cerebral hemorrhage and essential hypertension.

George Robert Cruickshank, Windsor, Ont., Canada; Victoria University Medical Department, Coburg, 1886; L.R.C.P., Edinburgh, Scotland, 1890; past president of the College of Physicians and Surgeons of Ontario; member of the Senate of the University of Toronto for many years; medical officer of health for Windsor from 1914 to 1919, and helped to organize the present board of health; in 1919 was president of the Ontario Health Officers Association; aged 80; died, October 8.

Roland Beatty Tupper ⊕ Fresno, Calif.; Cooper Medical College, San Francisco, 1910; at one time assistant clinical professor of medicine at his alma mater; member of the American College of Chest Physicians; served during the World War; formerly on the staff of St. Luke's Hospital, San Francisco; aged 54; on the staffs of the Fresno General Hospital and the Burnett Sanitarium, where he died, October 30, of coronary occlusion.

Henry Edward Menage, New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1892; member of the Louisiana State Medical Society and the American Academy of Dermatology and Syphilology; professor of dermatology emeritus at his alma mater; veteran of the Spanish-American War; formerly on the staff of the Charity Hospital; aged 68; died, October 22, of arteriosclerotic heart disease.

Samuel Jackson Pate, Woodville, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1905; member of the State Medical Association of Texas; past president of the Jefferson County Medical Society; served during the World War; on the staffs of the Hotel Dieu Hospital and St. Therese Hospital, Beaumont; aged 62; died, October 17, of chronic nephritis, myocarditis and hypertension.

Frederick Francis Andrews ⊕ Revere, Mass.; Harvard Medical School, Boston, 1905; for many years school physician; formerly member of the board of health; on the staffs of the Winthrop (Mass.) Community Hospital, Whidden Memorial Hospital, Everett, and the Chelsea (Mass.) Memorial Hospital; aged 68; died, November 5.

William A. Spurgeon, Muncie, Ind.; Physio-Medical College of Indiana, Indianapolis, 1875; member of the Indiana State Medical Association; past president of the Indiana State Board of Medical Registration and Examination and of the American Confederation of Reciprocating Medical Licensing Boards; aged 88; died, October 21.

Monroe T. Smith, Warren, Pa.; Medico-Chirurgical College of Philadelphia, 1889; member of the Medical Society of the State of Pennsylvania; past president of the Warren County Medical Society; for many years on the staff of the Warren General Hospital; aged 74; died, October 25, of coronary embolism.

Francis William Briggs ⊕ Havre, Mont.; State University of Iowa College of Medicine, Iowa City, 1905; member of the American Academy of Ophthalmology and Otolaryngology; on the staffs of the Sacred Heart and Deaconess hospitals; aged 66; died, October 27, in Great Falls, of heart disease.

Henry R. Krasnow, Chicago; Chicago College of Medicine and Surgery, 1914; instructor of dermatology at the University of Illinois College of Medicine; aged 57; on the staffs of the Research and Educational Hospital and the American Hospital, where he died, October 31, of coronary thrombosis.

Raymond Braxton Kicklighter, Glennville, Ga.; University of Georgia Medical Department, Augusta, 1928; member of the Medical Association of Georgia; served during the World War; aged 46; died, October 29, in the Veterans Administration Facility, Oteen, N. C., of tuberculosis.

Florence Gertrude Mikulski, Buffalo; University of Buffalo School of Medicine, 1924; member of the Medical Society of the State of New York and the American Society of Anesthetists; on the staffs of the Millard Fillmore and Lafayette General hospitals; aged 46; died, October 24.

Earle Haggett MacMichael, Englewood, Fla.; Harvard Medical School, Boston, 1910; served during the World War; member of the New England Society of Psychiatry; aged 56; died, October 27, in Venice of hypertensive heart disease, arteriosclerosis and arthritis deformans.

George J. Hess, Wayne, Neb.; Detroit College of Medicine, 1894; member of the Nebraska State Medical Association; also a pharmacist; president of the Wayne County Medical Society; aged 72; died, October 25, in a hospital at Norfolk of cerebral hemorrhage.

Clinton C. Tyrrell, Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1906; member of the Minnesota State Medical Association; served during the World War; aged 63; died, October 22, of chronic myocarditis and arteriosclerosis.

John Gilmer Reynolds, Chatham, Va.; Hospital College of Medicine, Louisville, Ky., 1904; member of the Medical Society of Virginia; aged 71; died, October 25, in the Memorial Hospital, Danville, of arteriosclerosis, myocarditis and bronchopneumonia.

Eb Nichols Gray, Houston, Texas; Jefferson Medical College of Philadelphia, 1883; member of the State Medical Association of Texas; on the staffs of the Memorial, Hermann and Jefferson Davis hospitals and St. Joseph's Infirmary; aged 79; died, October 19.

Charles Sumner Reed, Agency, Iowa; Drake University Medical Department, Des Moines, 1902; member of the Iowa

State Medical Society; past president of the Wapello County Medical Society; aged 70; died, October 4, of cerebral hemorrhage.

Preston Winford Pearson, Emory, Texas; Memphis (Tenn.) Hospital Medical College, 1903; member of the State Medical Association of Texas; past president of the Hunt-Rockwell-Rains Counties Medical Society; aged 57; died, October 12.

Wilbur Moate Scott ✠ Milledgeville, Ga.; University of Maryland School of Medicine, Baltimore, 1912; served during the World War; member of the Southeastern Surgical Congress; owner of the Scott Hospital; aged 49; was found dead, October 31.

William Bedwell Harrell Sr., Thomaston, Ala.; Louisville (Ky.) Medical College, 1905; member of the Medical Association of the State of Alabama; aged 59; died in October at a hospital in Birmingham of a severed artery, self inflicted.

William Alonzo Smith, Panther Burn, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; member of the Mississippi State Medical Association; aged 57; died, October 6, in the King's Daughters' Hospital, Greenville, of pneumonia.

James Harvey Hudson, Merrill, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1883; formerly member of the school board, mayor and postmaster; aged 81; died, October 24, of multiple sclerosis.

Edwin Cornue Hoff ✠ Detroit; Cleveland Homeopathic Medical College, 1901; fellow of the American College of Surgeons; aged 65; on the staff of the Grace Hospital where he died, October 23, of heart disease and prostatectomy.

Walter Wesley Sawyer, Elizabeth City, N. C.; University of Maryland School of Medicine, Baltimore, 1903; member of the Medical Society of the State of North Carolina; aged 60; died, October 20, of coronary thrombosis.

Nathan I. Kithcart, Columbia City, Ind.; Medical College of Ohio, Cincinnati, 1881; member of the Indiana State Medical Association; formerly secretary of the Whitley County Medical Society; aged 89; died, October 29, of myocarditis.

Albert Earl Sumner, Richmond Hill, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1894; consulting physician to the Roosevelt Hospital, New York; aged 73; died, October 31.

Owen F. Moran, Milledgeville, Ga.; Atlanta Medical College, 1888; member of the Medical Association of Georgia; formerly county commissioner of health; aged 73; died, October 31, of myocarditis and arteriosclerosis.

Francis Joseph Noonan, Troy, N. Y.; Albany Medical College, 1905; served during the World War; on the staff of the Troy Hospital; aged 59; died, October 18, of cerebral hemorrhage, arteriosclerosis and diabetes mellitus.

Bert Luther Kennedy, Dalton, Ga.; Birmingham (Ala.) Medical College, 1911; member of the Medical Association of Georgia; aged 59; died, October 17, in the Newell Sanitarium, Chattanooga, Tenn., of coronary occlusion.

John H. Heidelman, Ronan, Mont.; Cincinnati College of Medicine and Surgery, 1891; formerly a member of the Indian Service; aged 74; died, September 29, at the St. Patrick Hospital, Missoula, of coronary occlusion.

Melvin D. Hereford ✠ Staten Island, N. Y.; University of Kansas School of Medicine, Kansas City, Kan., 1922; served during the World War; on the staff of the Richmond Memorial Hospital; aged 43; died, October 25.

Henry Learen Applewhite, Archer City, Texas; Southern Methodist University Medical Department, Dallas, 1914; member of the State Medical Association of Texas; aged 53; died, September 6, in a hospital at Olney.

James P. Womack, Nashville, Tenn.; University of Tennessee Medical Department, Nashville, 1886; assistant to the chair in physiology at his alma mater, 1890-1891; aged 79; died, October 28, of cerebral hemorrhage.

Francis Joseph Harrington, Fall River, Mass.; Maryland College of Eclectic Medicine and Surgery, Baltimore, 1914; aged 47; was found dead, October 14, of heart disease and chronic dilatation of the esophagus.

William Armine Humphrey, Columbus, Ohio; Hahnemann Medical College and Hospital, Chicago, 1883; fellow of the American College of Surgeons; aged 80; died, October 30, of arteriosclerotic heart disease.

Horace Hampton Hilliard, Canton, Texas; Baylor University College of Medicine, Dallas, 1917; member of the State Medical Association of Texas; served during the World War; aged 50; died, October 14.

Harry Willard Waterous, Galva, Ill.; Rush Medical College, Chicago, 1885; member of the Illinois State Medical Society; aged 81; died, October 24, in East Pepperell, Mass., of coronary occlusion.

Bernard Weiss ✠ South Ozone Park, N. Y.; Long Island College Hospital, Brooklyn, 1929; on the staff of the Queens General Hospital, Jamaica; aged 36; died, October 20, of coronary thrombosis.

Arthur Wallace Winch, Sanford, Maine; Baltimore Medical College, 1906; served during the World War; aged 61; died, October 13, in the Deaconess Hospital, Boston, of pulmonary tuberculosis.

Victor Hugo Miller, Lakeland, Fla.; University of Louisville (Ky.) Medical Department, 1912; served during the World War; aged 53; died, October 16, in the Morrell Hospital of coronary thrombosis.

William Orville Wilkes, Waco, Texas; University Medical College of Kansas City, Mo., 1885; member of the State Medical Association of Texas; aged 77; died, October 17, of coronary sclerosis.

Roscoe Wesley Swan, Worcester, Mass.; Harvard Medical School, Boston, 1882; member of the Massachusetts Medical Society; aged 80; died, October 13, in the Holden (Mass.) District Hospital.

George Jackson Hill, Boston; Harvard Medical School, Boston, 1903; member of the Massachusetts Medical Society; formerly on the staff of the Children's Hospital; aged 61; died, October 29.

John Paul Hiebert ✠ Minneapolis; Northwestern University Medical School, Chicago, 1905; on the staffs of the Eitel, Abbott and Asbury hospitals; aged 63; died, October 11, of carcinoma of the pancreas.

John T. Iles, Ewing, Texas; University of Arkansas School of Medicine, Little Rock, 1911; aged 63; died, October 16, in the Angelina County Hospital, Lufkin, of cardiovascular renal disease.

Joseph O. King, Ridge, Md.; Baltimore University School of Medicine, 1895; member of the Medical and Chirurgical Faculty of Maryland; aged 67; died, October 31, of pulmonary tuberculosis.

Charlotte Margaretha Sekler Koester, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; aged 69; died, October 2, of pancreatitis.

Kary Gibbon Parker ✠ Mansfield, Ohio; Miami Medical College, Cincinnati, 1903; for many years on the staff of the Ohio State Reformatory; aged 65; died, October 24, of pneumonia.

John Roscoe Varney, Old Town, Maine; Baltimore Medical College, 1896; member of the Maine Medical Association; aged 77; died, October 25, of arteriosclerosis and pulmonary infarction.

Lloyd Thomas Reed, Gravity, Iowa; St. Louis College of Physicians and Surgeons, 1900; member of the Iowa State Medical Society; aged 62; died, October 17, of coronary occlusion.

Isaac H. Treece, Findlay, Ohio; Eclectic Medical Institute, Cincinnati, 1887; aged 77; died, October 24, in the Findlay Hospital of a wound received when his gun accidentally exploded.

Abraham Lincoln Trevaskis, Turtle Creek, Pa.; Starling Medical College, Columbus, 1892; member of the Medical Society of the State of Pennsylvania; aged 80; died, October 28.

Henry H. Clark, Minneapolis; College of Physicians and Surgeons of Chicago, 1893; member of the Minnesota State Medical Association; aged 76; died, October 31, of carcinomatosis.

Charles Joel Sage ✠ New York; University of Vermont College of Medicine, Burlington, 1931; aged 36; died, October 18, in the Mount Sinai Hospital of acute myelogenous leukemia.

Jonas Ruby, Chicago; Chicago College of Medicine and Surgery, 1917; for many years school health officer; aged 54; died, October 21, in the American Hospital of coronary occlusion.

James D. Stuart, Washington, D. C.; Columbian University Medical Department, Washington, 1892; member of the Medical Society of the District of Columbia; aged 75; died, October 18.

Moses James Ferguson, Mexico, D. F., Mexico; University of Nashville (Tenn.) Medical Department, 1905; aged 58; died in October of injuries received in an automobile accident.

George A. Noon, Listie, Pa.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1890; member of the Medical Society of the State of Pennsylvania; aged 81; died, October 12.

Albert Sidney Stemler, Washington C. H., Ohio; Eclectic Medical Institute, Cincinnati, 1898; member of the Ohio State Medical Association; aged 66; died in October in Cleveland.

Willie Gregor Spires, Gaskin, Fla.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1916; formerly member of the county school board; aged 55; died, October 19.

Jesse Braxton Higgins, Indianapolis; Fort Wayne (Ind.) College of Medicine, 1901; aged 62; died, October 27, in the Veterans Administration Facility of coronary disease.

Frank Horan Gunn, Eau Claire, Wis.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1895; aged 68; died, October 13, of arteriosclerotic heart disease.

Napoleon J. Caron, South Hero, Vt.; Laval University Faculty of Medicine, Quebec, Canada, 1899; aged 69; died, October 23, of carcinoma of the lungs with metastasis.

John Walter Herritage Jr., St. Louis; Meharry Medical College of Walden University, Nashville, Tenn., 1938; aged 28; died, October 6, of pulmonary tuberculosis.

Lloyd Howe Mott, Los Angeles (licensed in Oregon in 1912); on the staff of the Veterans Administration Facility, West Los Angeles; aged 53; died in October.

George E. French ⊕ Elyria, Ohio; Western Reserve University Medical Department, Cleveland, 1888; for many years city health officer; aged 76; died, October 30.

William M. Van Der Volgen, Seattle; Kentucky School of Medicine, Louisville, 1877; Medical College of Ohio, Cincinnati, 1887; aged 84; died in October.

Reginald Myron Wildish ⊕ Webster City, Iowa; University of Nebraska College of Medicine, Omaha, 1911; aged 55; died, September 30, of cardiac embolism.

William James Pillsbury, Baltimore; University of Maryland School of Medicine, Baltimore, 1889; aged 72; died, October 29, of cerebral hemorrhage.

Henry Andrew Lile ⊕ Harlingen, Texas; Barnes Medical College, St. Louis, 1899; aged 66; died, October 21, in the Masonic Hospital, Cherokee, Okla.

Lawrence Henry Oliver, Waupun, Wis.; Marquette University School of Medicine, Milwaukee, 1916; aged 54; died, October 30, of coronary occlusion.

George Tapscott Snead, Pungo, Va.; Medical College of Virginia, Richmond, 1880; formerly member of the state legislature; aged 83; died, October 30.

Walter A. Jenkins, Church Point, La.; Louisville (Ky.) Medical College, 1887; aged 80; died, October 15, of diabetes mellitus, nephritis and myocarditis.

Spencer De Witt Guy ⊕ Lansing, Mich.; Rush Medical College, Chicago, 1917; served during the World War; aged 47; died, October 26, of pellagra.

Edwin B. Boots ⊕ Terre Haute, Ind.; Indiana University School of Medicine, Indianapolis, 1930; aged 40; died, October 7, of a gunshot wound.

George Henry Belding, Milwaukee; Milwaukee Medical College, 1903; formerly a dentist; aged 77; died, September 15, of chronic endocarditis.

Alexander Neil MacLeod, Winnipeg, Man., Canada; Manitoba Medical College, Winnipeg, 1893; aged 72; died, October 11, of cerebral hemorrhage.

William McKee Thome, Salem, Ore.; Jefferson Medical College of Philadelphia, 1897; aged 71; died, October 22, of carcinoma of the prostate.

Isabella Holdom, Minneapolis; Michigan College of Medicine and Surgery, Detroit, 1897; aged 81; died, October 23, of cardiac decompensation.

John Earle Jenner, Vancouver, B. C., Canada; Trinity Medical College, Toronto, 1883; L.R.C.P., London, 1883; aged 83; died, October 28.

William Herbert Marshall, Weiser, Idaho; Trinity Medical College, Toronto, Ont., Canada, 1899; aged 66; died, October 18, in Boise.

Thomas Benjamin Smith, Bracey, Va.; Jefferson Medical College of Philadelphia, 1881; aged 81; died, October 15, of cerebral hemorrhage.

George L. Shoemaker, Jennings, La.; Chicago Homeopathic Medical College, 1891; aged 80; died, October 21, of coronary thrombosis.

William Henry Loechner, Omaha; Omaha Medical College, 1901; aged 63; died, October 28, of carcinoma of the head of the pancreas.

Charles Huston Minor, New York; Ohio State University College of Homeopathic Medicine, Columbus, 1920; aged 46; died, September 25.

Samuel S. Guerrant, Callaway, Va.; Medical Department of Tulane University of Louisiana, New Orleans, 1891; aged 73; died, October 28.

Morgan Biddle Jennings, Streator, Ill.; Rush Medical College, Chicago, 1886; aged 77; died, November 16, in St. Mary's Hospital.

James Thompson Longest, Pontotoc, Miss.; University of Tennessee Medical Department, Nashville, 1903; aged 68; died, October 24.

Howard Cousins Fairbanks ⊕ Tonawanda, N. Y.; University of Buffalo School of Medicine, 1909; aged 54; died, October 13.

Alvin Dennett Holmes, Hudson, Mass.; Medical School of Maine, Portland, 1884; aged 84; died, October 24, of chronic myocarditis.

Walter Jay Insley, Columbus, Ohio; Bennett College of Eclectic Medicine and Surgery, Chicago, 1887; aged 83; died, October 26.

Walter Bryant Guy, St. Augustine, Fla.; Boston University School of Medicine, 1899; aged 70; died, October 3, of coronary thrombosis.

William James Brown, Boston; Tufts College Medical School, Boston, 1906; aged 60; died, September 15, in Plymouth.

Walter A. Gatlin, Paris, Texas; Memphis (Tenn.) Hospital Medical College, 1902; aged 67; died, October 25, of coronary occlusion.

Richard W. Carter, Chicago; Fort Wayne (Ind.) College of Medicine, 1893; aged 70; died, October 25, of chronic myocarditis.

Archibald M. McKennon, Clarksville, Ark.; Jefferson Medical College of Philadelphia, 1874; aged 88; died, October 23.

Francis Edward Carroll, Boston; Harvard Medical School, Boston, 1890; aged 78; died, September 10, in Saugus.

William Douglas Swan, Hamilton, Ont.; University of Toronto Faculty of Medicine, 1921; aged 50; died, October 23.

Alexander Douglas Taylor, Daytona Beach, Fla.; Rush Medical College, Chicago, 1875; aged 86; died, October 5.

Andrew J. Hays, Weslaco, Texas; Keokuk (Iowa) Medical College, 1891; aged 79; died, October 15, of myocarditis.

William Tecumseh Pittman, Spickard, Mo.; Rush Medical College, Chicago, 1892; aged 70; died, October 31.

Joseph A. Roth, Chicago; Harvey Medical College, Chicago, 1905; aged 66; died, October 14, of diabetes mellitus.

Eugene Clair Wasson, Cambridge Springs, Pa.; Baltimore Medical College, 1905; aged 62; died, October 19.

Thomas Z. Clower, Moreland, Ga.; Southern Medical College, Atlanta, 1893; aged 70; died, October 5.

George William May ⊕ Manchester, Conn.; Milwaukee Medical College, 1895; aged 80; died, October 23.

James Griffin Elrod, Dutton, Ala.; Chattanooga (Tenn.) Medical College, 1902; aged 82; died, October 29.

Victoria Sarah Ernst, Bridgewater, N. S., Canada; Halifax Medical College, 1900; aged 84; died, October 4.

Joseph Ira Esch, La Farge, Wis.; Eclectic Medical Institute, Cincinnati, 1898; aged 71; died in October.

CORRECTION

Dr. Pearson Is Not Dead.—The obituary notice of Dr. Charles Birdsall Pearson of Anaheim, Calif., which appeared in THE JOURNAL, November 30, page 1905, was erroneous. Our source of information was a clipping from the Grand Blanc, Mich., *Press*, dated Oct. 10, 1940.

Correspondence

THE EFFECT OF ALCOHOL ON DRIVING SKILL

To the Editor:—The recent article "The Effect of Alcohol on Driving Skill" (THE JOURNAL, November 9, p. 1600) brings out a number of interesting facts but may lead to erroneous conclusions if not carefully scrutinized. An ingenious test of driving skill, including both steering and braking, showed that the two skills were more closely correlated than either or both with the exact concentration of alcohol in the blood stream. However, it should be noted that the subjects showed a remarkably similar concentration of alcohol in the blood after the test dose, in no instance varying by more than 0.03 per cent from the average concentration to be expected (chart 1) and almost all lying in the zone characterized by the committees of the American Medical Association and the National Safety Council, as well as most students of the subject, as of "suggestive" or "presumptive" rather than of "conclusive" or "prima facie" significance. Even in this narrow zone, the coefficient of correlation of 0.485, more than six times its probable error, is impressive. If the data had extended over the higher ranges, in which the chemical test is conclusive, as well as over the lower ranges, in which it distinguishes so usefully between the "had been drinking" and the "under the influence" group, a much higher degree of correlation would have undoubtedly appeared. As a matter of fact, the only four persons shown in chart 2 with sufficient alcoholic concentration in the blood to have been convicted by the chemical test alone all showed more than 15 per cent loss of efficiency in driving ability by the tests here reported.

The tests used appear to have been well calculated to bring out differences in driving skill, resulting from changes in reaction time and neuromuscular coordination. As emphasized in the preliminary report of the committee of the American Medical Association on this subject, the early effects of alcohol which may lead to automobile accidents are rather in the sphere of judgment, discretion and disposition than of the more mechanical skills here tested. The slightly intoxicated expert chauffeur may be much better able than the sober occasional driver to pass tests in steering and braking abilities but may also be more apt to take chances or be careless when not consciously being tested. The subject's fallacious impression that skill is improved during the influence of alcohol, noted here as in previous studies, also leads to greater dangers.

The contention that the chemical tests for intoxication penalize the drinking rather than the drunken driver is just the reverse of the facts. It is just the finding that a driver who has been drinking but has less than 0.05 per cent of alcohol in the blood generally fails to show other evidences of intoxication, while the one with more than 0.15 per cent may be shown to be under the influence if sufficiently examined, which makes this test of differential value, as compared with merely smelling the breath or showing the bottle.

It is still conceivable that a person might be found who can have a concentration of alcohol in the blood stream above 0.15 per cent and still fail to show any evidence of the effect of the alcohol on the tissues. Despite thousands of tests, however, and public appeals for the discovery of such person, no such instance has yet been verified. The search should be continued, as further study of such a case might be of great value for our understanding of the nature of tolerance to alcohol. Its occurrence, however, is still unproved.

If one disregards their comments and conclusions, the work of Newman and Fletcher may be accepted as a valuable contribution toward the evaluation of the status of the "borderline case" of the driver with a concentration of alcohol between 0.05 and 0.15 per cent. Practically every worker in this field, as well as the committees of the American Medical Association and the National Safety Council, have urged the use of other evidence in addition to, and in support of, the value of the chemical test, and the performance of the latter in duplicate, or with different samples, in questionable cases. The possibility of technical errors in the performance of the tests, as well as still unknown possibilities in their interpretation, should not be overlooked. The article on false positive serologic tests for syphilis in THE JOURNAL just following the paper by Newman and Fletcher, however, indicates how a similar valuable test in another field in medicine may be safeguarded rather than ignored. Further studies of tolerance to alcohol and the factors involved in automobile accidents are still greatly to be desired. At present, however, it may be emphatically reiterated that the determination of the alcoholic concentration of the breath or body fluids remains the most reliable single factor in arriving at a correct conclusion as to the degree of intoxication.

EMIL BOGEN, M.D., Olive View, Calif.

To the Editor:—The recent paper on "The Effect of Alcohol on Driving Skill" by Newman and Fletcher (THE JOURNAL, November 9, p. 1600) presents conclusions which are at variance with the majority of scientific investigations on the effects of alcohol. Their report demonstrates the extreme confusion which may result from varying conceptions of the terms "drunk" and "intoxicated." Some writers have maintained that any demonstrable deviation from normal behavior produced by alcohol constitutes alcoholic intoxication. By such a rigid definition most persons may be considered intoxicated following exceedingly small amounts of alcohol such as are contained in a single cocktail or "highball." The opposite extreme is indicated by the criterion often employed by bartenders in determining whether or not a customer may legally be sold further quantities of liquor. This view is perhaps best illustrated by the old barroom quatrain:

He is *not* drunk who from the floor
Can rise again and drink once more.
But he *is* drunk who prostrate lies
And can neither drink nor rise.

There is a world of difference between these two extremes in defining the term "drunk." When Newman and Fletcher state "Public sentiment is definitely against the drunken driver but not against the drinking driver," all can agree with them in principle. The really important question which must be answered is When does a drinking driver become a drunken driver? Certainly it is long before he reaches the staggering stage of alcoholic intoxication. As was suggested in THE JOURNAL ("The Subintoxicated Driver," May 2, 1936, p. 1580) four years ago, serious impairment of driving ability occurs before the ordinary indications of "intoxication" are observable; hence the use of the term "subintoxicated driver." The public associates the term "drunk" with a stage of alcoholic intoxication characterized by staggering gait and confused or slurred speech. Apparently on such a basis Jetter (cited by Newman and Fletcher in support of their thesis) made his clinical diagnosis of acute alcoholic intoxication. Such standards, while entirely suitable for purposes of hospital classification, are hardly adequate for diagnosis of the influence of alcohol on motorists.

The use of the term "under the influence of alcohol" seems to avoid the many deep-seated connotations which, through long usage, adhere to such words as "drunk" or "intoxicated." This condition might be defined as that state at which the effect of alcohol renders a person unfit to perform the particular task which he is attempting. To evaluate fairly the influence of alcohol requires one to take into consideration not only the effects of the alcohol which is circulating through

the body of that person but also the type of activity in which he is engaged. Thus a man may have taken several "highballs" and seated himself in his home to listen to a radio program. For such a purpose he might be considered to be entirely sober. But if this same man were to undertake a task involving quick and accurate response to stimuli and the use of sound judgment, such as driving a high powered automobile through crowded city streets, he would be fairly classified as "under the influence of alcohol." The loose use of the terms "drunk" and "intoxicated" gives rise to much unnecessary confusion.

The psychologic tests of driving skill reported by Newman and Fletcher illustrate the difficulty in setting up an experimental routine which will measure the desired variable to the exclusion of all others. With reference to tests on the influence of alcohol, these difficulties have been admirably stated by Jellinek and McFarland (Analysis of Psychological Experiments on the Effects of Alcohol, *Quart. J. Studies on Alcohol* **1**:272 [Sept.] 1940). Apparently what Newman and Fletcher have measured was impairment of driving skill due to the effect of alcohol plus improvement due to practice. Little wonder, therefore, that they find such poor correlation between alcohol concentration in the blood and their "loss of driving skill." The most eloquent practical demonstration of the correlation between alcohol content of body fluids and driving skill is to be found in the Evanston survey (Holcomb, R. L.: Alcohol in Relation to Traffic Accidents, THE JOURNAL, Sept. 17, 1938, p. 1076). A statistical study of the data was made to determine a motorist's chances of finding himself in an Evanston hospital following an automobile accident. Depending on the concentration of alcohol in the blood stream, these probabilities were as follows:

Alcohol in Blood, per Cent	Chances of Hospitalization Following an Automobile Accident
0	1
Less than 0.07	3
0.07 to 0.11	5
0.11 to 0.15	15
Over 0.15	55

It is not reasonable to expect perfect correlation between the dose of any drug and the effect which it produces (Nelson, E. E.: Variability in Response to Drugs, THE JOURNAL, Oct. 7, 1939, p. 1373). However, within the limits of normal biologic variation which my experience has indicated to be about 10 to 15 per cent in the case of alcohol (McNally, W. D.: Toxicology, Chicago, Industrial Medicine, 1937, p. 659), all persons, regardless of previous experience in the use of alcohol, are equally under the influence of alcohol when they have the same concentration of alcohol in their circulating blood. That determinations of alcohol in the blood leave much to be desired cannot be denied. However, they do serve as an excellent adjunct in the correct interpretation of less quantitative clinical indications of the influence of alcohol. Until better practical and more reliable methods can be found, one may safely continue to employ the methods recommended by the American Medical Association Committee to Study Motor Vehicle Accidents (THE JOURNAL, May 27, 1939, p. 2165) and embodied in the National Safety Council's program for safe driving practice.

The use of our highways is not an inherent individual right such as the rights of free speech, free assembly and freedom of worship. It is a privilege conferred by the communities in which we live and may be legally abridged in any way which seems in the interest of public safety and welfare. Society must be free to take effective steps in controlling the ever mounting toll of deaths and injuries due to highway accidents.

C. W. MUEHLBERGER, PH.D., Chicago.
Coroner's Toxicologist, Cook County
Coroner's Laboratory.

To the Editor:—In the article by Newman and Fletcher, "The Effect of Alcohol on Driving Skill" (THE JOURNAL, Nov. 9, 1940, p. 1600), are certain discrepancies which might not be perceived.

The authors give experimental data which apparently justify their attack on the "injustice" of the figure of 0.15 per cent alcohol in the blood, which has been set by committees of both the American Medical Association and the National Safety Council as the point at which 100 per cent of persons "tolerant" or otherwise suffer a definite impairment in their driving ability, to the extent that it comes within the meaning of most state laws concerning drunken driving.

They state that the purpose of their experimental work was to investigate the correlation between impairment of driving ability and the 0.15 per cent concentration of alcohol in the blood. Their data of ninety-eight trials on 65 subjects are presented in the form of a pinpoint chart percentage of impairment over normal performance against concentrations of alcohol in the blood. They say that it shows a poor correlation between the two. It does just that and nothing more. The validity of the recommended figure of 0.15 per cent remains unaffected, for the following reasons:

1. Eighty results were between approximately 0.06 and 0.12 per cent, nine between 0.12 and 0.14 per cent, one close to 0.15 per cent and three above 0.15 per cent. The majority of their results were therefore obtained at concentrations much below 0.15 per cent. The four at or above 0.15 per cent prove nothing.

2. The fifteen minute trial periods preceding the actual tests were totally inadequate to eliminate any progressive improvement from this factor. A fifteen minute trial could not possibly have resulted in a plateau of performance for each subject.

3. It is a well known fact that many persons with alcohol concentrations of the blood below 0.15 per cent have a degree of unaffected will power which they can summon to their aid, if there is a reason for them to do so, to compensate to a considerable degree for the effect of the alcohol. This factor in itself may reasonably be held accountable for the poor correlation that the authors found. It is difficult to avoid this compensatory effect in any study which involves performance observation at low concentrations of alcohol. The subject cannot help but be aware that he is expected to make as good a showing as he can. At these low concentrations the occasional unquestionable better performance in such tests is in my opinion due entirely to a compensatory effort over and above that needed to counteract the alcohol. The subject gives a better performance not because of any bettering effect of the alcohol but in spite of it.

It is my sincere belief, based on nearly four years of observing and running blood and urine alcohol tests on actual drunken drivers to a total of between 300 and 400 that, if by some unattainable means every drunken driver's physical condition could be observed unknown to him, no disagreements between concentrations and effects would ever be observed. One sees practically perfect agreements at higher concentrations, because in practically all persons this mechanism then either no longer functions or it is not powerful enough to overcome all the effects of the alcohol.

Whether this occasional exhibition of compensatory mechanism, fairly frequent at low concentrations but becoming rare at higher ones, is due to a progressive loss in will power (apace with progressive impairment in other functions), to a variability in the development of individual will power or to a complex interplay of the two is difficult to say. The important point to keep in mind is that intoxicated persons do not make any effort to exert this compensatory mechanism while driving a car. It never occurs until the person is arrested and is under observa-

tion for his condition. One must remember that, in the ultimate analysis, blood and urine tests are made to determine the stage of intoxication of the subject while he was driving a car and not necessarily after various extraneous factors which unavoidably follow his arrest have entered the picture. These factors are well known to be able to modify the relation between the concentration of alcohol in the blood and the observable effect.

No one has yet succeeded in devising an apparatus to be used in the laboratory in testing driving ability which will take into account all factors, including judgment and estimation of risks, which play a part in determining what an intoxicated person will do, or fails to do, when behind the wheel of a car.

Up to now in only one known instance in the United States has such a study been made wherein the subjects actually drove a car. This was reported in the *Pennsylvania Medical Journal* for December 1932 by Drs. H. A. Heise, Benjamin Halporn and Alfred G. Dietze. The results were considerably different than those of Dr. Newman and Mr. Fletcher. In Dresden, Germany (THE JOURNAL, May 7, 1938, p. 1617), a series of tests were made on a large number of volunteers. At a concentration of 100 mg. of alcohol per hundred cubic centimeters of blood, there were 87 per cent of the drivers incapacitated and at 140 mg. 100 per cent.

Newman and Fletcher should repeat their experiment and see to it that the following points are observed: 1. Their subjects should be given doses of alcohol large enough to insure their blood alcohol being at or slightly above 0.15 per cent. 2. Care should be taken that the factor of compensation is eliminated as much as possible by using other than medical students and physicians as subjects and avoiding any hint to the subject, intentional or otherwise, that he is expected to try to drive better because of the alcohol. No suggestion (such as that of a signaling green light) should be given the subject that his alinement of radiator cap with the truck is faulty other than that given by his own judgment. 3. A longer practice period should be given and a plateau definitely established before the alcohol is administered. If this is done, my opinion is that Dr. Newman will obtain a considerably different result.

D. F. DAVIS,
City Health Department, Lincoln, Neb.

To the Editor: — The article "The Effect of Alcohol on Driving Skill" by Newman and Fletcher (THE JOURNAL, November 9, p. 1600), questions the value of chemical tests for intoxication. This paper demands an answer, since the conclusions of the authors are warranted neither from their own experimental data nor from their interpretation of the writings of others.

The authors direct their attack particularly to the recommendations of the Committee on Tests for Intoxication of the National Safety Council, and incidentally to the 1939 Report of the Committee of the American Medical Association for the Study of Problems of Motor Vehicle Accidents. These committees have agreed that certain levels of alcohol in the blood or their equivalents in other body fluids are associated with a definite loss of that clearness of intellect and self control which an individual would normally possess. Although the committees realize that there is no minimal figure that can be set at which there will be no effect from alcohol, they agree that all persons are definitely inferior to their normal capabilities when the alcohol concentration exceeds 0.15 per cent. (To reach a blood alcohol concentration of 0.15 per cent, the average sized adult must fail to oxidize from 3 to 4 ounces [90 to 120 cc.] of absolute alcohol.)

The reason for the disagreement is obviously the failure of Newman and Fletcher to realize that there is a vast difference between the poorly defined terms of drunkenness and intoxication, and the well defined "under the influence of alcohol."

The National Safety Council Committee recommends that trial courts adopt the definition of the phrase "under the influence of alcohol" as laid down by the Supreme Court of Arizona:

> "The expression 'under the influence of intoxicating liquor' covers not only all the well known and easily recognized conditions and degrees of intoxication but any abnormal mental or physical condition which is the result of indulging in any degree in intoxicating liquors, and which tends to deprive him of that clearness of intellect and control of himself which he would otherwise possess. If the ability of the driver of an automobile has been lessened in the slightest degree by the use of intoxicating liquors, then the driver is deemed to be under the influence of intoxicating liquor. The mere fact that the driver has taken a drink does not place him under the ban of the statute unless such drink has some influence upon him lessening in some degree his ability to handle said automobile."—*Steffani* v. *State, 42 Pac. (2nd) 615.*

The fact that a skilled driver under the influence of alcohol may be able to drive better than an ordinary sober person does not in any way clash with the definition.

The published results of the authors' experiments, involving the use of a machine which measures steering ability and reaction time, do not refute the conclusions of the committees of the American Medical Association and National Safety Council. On the contrary, the four persons whose blood alcohol concentrations exceeded 0.15 per cent all showed 16 per cent or more loss of efficiency, which would definitely place them "under the influence."

The authors state that performance of their test of simple steering is a better criterion of intoxication than is blood alcohol. My experiments along similar lines (Medicolegal Aspects of Drunkenness, *Pennsylvania M. J.* **36**:190 [Dec.] 1932) but under actual driving conditions indicated that the ability to perform the routine of driving was not always obviously impaired in persons who were under the influence of alcohol according to chemical tests. However, the performances of acts which were not routine, such as backing the car and manipulations demanding judgment, were poorly performed. A simple incident is responsible for abandonment of this type of test: a truck swerved across the path of the test car, narrowly avoiding a collision. When I said to the driver, who at that time tested about 0.13 per cent, "Say, wasn't that a narrow escape from that truck?" he looked at me with an expressionless face, saying, "What truck?" After this incident, less dangerous experiments involving skill, judgment and intelligence were instituted. By these tests it was a simple matter to demonstrate definite impairment in judgment and personality long before coordination was affected. In all my experiments, involving more than 200 persons, no one was found who was able to reach a blood alcohol concentration of 0.10 per cent without showing definite changes for the worse.

The conclusions of the authors are not warranted from their interpretation of the writing of Bogen (Drunkenness: A Quantitative Study of Acute Alcoholic Intoxication, THE JOURNAL, Oct. 29, 1927, p. 1508), himself a member of the Committee on Tests for Intoxication of the National Safety Council. Bogen reports the cases of persons who were adjudged intoxicated or drunk and not persons who were proved to be "under the influence."

Jetter's subjects (Studies in Alcohol, *Am. J. M. Sc.* **196**:475, 487 [Oct.] 1938) were adjudged intoxicated by a criterion which he himself set. In a recent article (The Chemical and Clinical Diagnosis of Acute Alcoholism, *New England J. Med.* **221**:1019 [Dec. 28] 1939) he makes his position clear:

> While only 50 per cent of cases in a group of habitual drinkers will be clinically intoxicated at a blood alcohol level of 0.15 Gm. per 100 cc., sufficient impairment of faculties will be present in even this type of individual to make him a menace as a driver.

Finally, I heartily disagree with the authors' implication that persons of greater skill than the average should not be penalized for their only offense of having alcohol in their blood stream. They would condone the resulting loss of driving

skill as long as the drivers managed to stay above "minimum standards of skill." They forget that the average driving skill results in a slaughter of more than 30,000 people in this country each year and that the superior driver has no legal or moral right to lower his efficiency toward the average.

HERMAN A. HEISE, M.D., Milwaukee.
Chairman, Committee of the American Medical Association to Study Problems of Motor Vehicle Accidents.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SERUM FOR POLIOMYELITIS

***To the Editor:*—What is the present status of convalescent serum in the treatment of anterior poliomyelitis?**

J. G. Woodin, M.D., Grand Island, Neb.

ANSWER.—A simple and unchallenged answer cannot be given on the beneficial effect of convalescent serum in the treatment of acute anterior poliomyelitis. The reasons lie somewhat in the variability of the disease itself and, as in other acute infectious diseases, in the fact that the disease is self limiting. Although the early workers in this field were unanimous in stating that convalescent serum tended to prevent the spread of paralysis and aided in the recovery of paralysis, present day workers view this early opinion with skepticism. At present the matter is to be considered somewhat undecided but with the potential field of usefulness of serum markedly narrowed.

Reaction against the wholesale indiscriminate use of convalescent serum dates from the report of Park on the New York epidemic of 1931 (Therapeutic Use of Antipoliomyelitis Serum in Preparalytic Cases of Poliomyelitis, THE JOURNAL, Sept. 24, 1932, p. 1051; *New York State J. Med.* **33**:91 [Jan. 15] 1933). This author reported on the serum treatment of half of the patients from a group of 927 in the preparalytic stage. The amount of paralysis judged by muscle examinations made shortly after the administration of serum and six months later showed no difference between the group that received serum and that which had received none. The data from this report were questioned by many workers in the field because alternate cases were not treated and serum was given to those seen late in the natural course of the preparalytic disease. It has since been shown that patients in the preparalytic stage, seen two or more days after the onset of paralysis, are already selected naturally and are destined to have little paralysis. The situation is further complicated by the fact that a large share of all cases diagnosable in the "preparalytic state" are actually nonparalytic cases; 71.5 per cent of 531 patients according to one published review (Harmon, P. H.: Poliomyelitis: Experimental and Theoretical Basis for Serum Therapy, *Am. J. Dis. Child.* **47**:1179 [June] 1934). Harmon also failed to find statistical evidence for the beneficial use of convalescent serum. The incidence of paralysis and the apparent prevention of paralysis by serum were the same according to these statistics regardless of whether the serum used was convalescent serum, the antistreptococcus horse serum of Rosenow or "normal" human serum, which contains antiviral antibodies active in the test tube. Likewise, Kramer, Aycock, Solomon and Thenebe (Convalescent Serum Therapy in Preparalytic Poliomyelitis, *New England J. Med.* **206**:432 [March 3] 1932) in the 1931 epidemic in Connecticut failed to find any difference in a control group of patients who did not receive convalescent serum and a similar group of patients who had received this agent.

The majority of workers have preferred to continue their observations. Convalescent serum admittedly does no harm and it has not yet been proved that it is valueless. Some favorable results have been recorded in recent years. Cowie, Parsons and Lowenberg have reported no residual paralysis in 80 preparalytic cases treated with both human convalescent serum and transfusions from "normal" adults. They also reported symptomatic improvement in certain paralytic cases. However, that serum was responsible solely for this turn of events must be viewed with skepticism in view of the well known tendency of the disease to halt spontaneously and suddenly in the face of apparent advancing paralysis (Clinicopathologic Observations on Infantile Paralysis: Report of 125 Acute Cases with Special Reference to the Therapeutic Use of Convalescent and Adult Blood Transfusions, *Ann. Int. Med.* **8**:521 [Nov.] 1934).

The most continuous experience with the use in convalescent serum in the treatment of this disease has been that of pediatricians and public health workers in the state of Illinois. The last official report originating from this source was that of Levinson (Poliomyelitis in the Chicago Area, *Illinois M. J.* **70**:296 [Sept.] 1936). This author reported on the treatment of 149 preparalytic cases occurring in Chicago between 1931 and 1935. In the 1936 epidemic a mortality rate of 39 per cent was reported in bulbar cases (the mortality in untreated cases was 90 per cent). Only 8 patients from 53 preparalytic cases became paralyzed after serum was administered. The mortality in the latter group was zero and only 2 had slight residual paralysis. While the incidence of paralysis in this group of preparalytic cases was not dissimilar to those not receiving serum, it should be pointed out that the incidence of residual paralysis was practically zero. A recent report emanating from California (Geiger, J. C.; Burlingame, R. W., and Miller, R. C.: Convalescent Serum in Acute Anterior Poliomyelitis: Report of a Study of 168 Patients, 69 Treated, 98 Untreated, *California & West. Med.* **51**:303 [Nov.] 1939) states that "the cases with entrance paralysis show little or no variation between treated and untreated in percentage in partial or complete recovery or death. Among those considered early cases, but with entrance weakness, the percentages of partial or complete recovery showed equally small or no variation in the treated and untreated. The early cases with no weakness or paralysis, however, indicate that a different viewpoint can be stressed. The preparalytic cases (27), when treated with convalescent serum, recovered without any residual paralysis. Therefore, in this series of cases of this type, or in early cases of acute anterior poliomyelitis with clinical and laboratory evidence substantiating the diagnosis, it would appear that convalescent serum is of benefit."

All the experimental evidence deduced from the use of convalescent human and monkey antiserum in the disease in monkeys clearly shows that the experimental disease is not benefited by serum. Such evidence should not be considered in evaluating the results in man, as the simian disease is entirely different in its onset, course and outcome. The disease in man is notoriously more variable and more mild both in extent of paralysis and in mortality.

The aggregate of opinion in recent years, as evidenced by the opinions and quotations given, would favor the use of human convalescent serum or transfusions from at least two or three normal adult blood donors during the preparalytic stage, while in cases of early paralysis in which the paralysis has ceased to advance and the temperature has dropped to normal serum should not be used. There are those who continue to use serum in early paralytic poliomyelitis, but no evidence can be said to favor such a procedure. From the practical point of view, it must be pointed out that the differentiation between preparalytic poliomyelitis and the early paralytic stages of this disease is exceedingly difficult.

LOCAL TREATMENT OF NASOPHARYNX IN "INFLUENZA"

***To the Editor:*—For the past two years I have noted a vesicular pharyngitis quite regularly in patients having the classic symptoms of influenza. This observation has been described as frequently accompanying the nasal pharyngitis that results from influenza. Is there any local treatment other than ephedrine shrinkage of the nasal pharynx and local application of silver salts that might be more specific as a remedy for the cough and gastrointestinal irritation that accompanies this lesion?**

Henry E. Davidson, M.D., Lead, S. D.

ANSWER.—The use of weak ephedrine solutions in the nose by means of drops, use of an atomizer or following the recommendations of Proetz, is a useful method of treating the rhinitis and rhinopharyngitis following the so-called "flu." The vesicles, after they have ruptured, may be treated by the application of silver salts together with hot nonirritating gargles. To the extent that the reduction of nasal secretion prevents the cough which is due to purulent matter dropping into the larynx and trachea, the cough will be improved. That part of the cough which is due to a laryngotracheitis should be dealt with by the use of mixtures containing codeine, by steam inhalations, bed rest and the like.

The gastrointestinal irritation is probably not due to the local nose and throat condition but is a part of the general picture and has to be dealt with in a common sense manner. This calls for a proper bland diet, the avoidance of drastic cathartics and similar rational measures.

MEDICAL EXAMINATIONS OF FOOD HANDLERS

To the Editor:—Please advise me whether an examination of feces is desirable on food handlers in an institution where 1,700 young women eat in three large dining halls and where the following public health measures are carried out: complete examination of all food handlers, laborers and maids, including routine roentgen examinations of the chest, urinalysis and blood agglutination tests for typhoid, proteus, tularemia, abortus and the paratyphoid groups. We have never made any examination of stool specimens and accordingly I am asking your advice as to the advisability of this practice. We are anxious to take every precaution to insure the health of our people. I might add that the dishes are boiled under high pressure in all eating places, including all tea rooms about the campus, and that all food handlers have special instructions about cleansing hands, finger nails and their bodies in general.

William B. Brown, M.D., Columbia, Mo.

ANSWER.—In general, routine examination of food handlers in large numbers is an expensive procedure. A single stool examination gives little information. It is not unusual to have a number of negative stool cultures followed by a positive culture in the case of a typhoid carrier. In an institution where every possible protection is desired and, especially, if the turnover in employees is not great, routine examination of stools is of some value. The limitations of the possibilities of detecting cases or carriers from a single examination must be remembered, however. If there is a history of typhoid it is desirable that repeated stool cultures be made.

From the point of view of protection of those served by the employees, little could be expected of the agglutination tests for typhoid, proteus (typhus fever, Rocky Mountain spotted fever), tularemia, undulant fever and paratyphoid. With the exception of typhoid and paratyphoid fever, direct transmission from patient to patient either does not occur in these diseases or is an insignificant factor in their spread.

The agglutination test is of little value in the detection of typhoid carriers. Probably the education of food handlers is the most important disease prevention factor. Food handlers should have knowledge of the practical facts concerning the transmission of communicable diseases and should have medical attention available for the investigation of any signs of illness.

AMENORRHEA

To the Editor:—A white woman aged 26, married, weighing 106 pounds (48 Kg.) complains of small and poorly developed breasts. She says that they were well developed seven years ago. The menses began at 13, were regular every twenty-eight days and lasted five or six days. There was no dysmenorrhea. She had a miscarriage at three and one-half months eight years ago, an appendectomy seven years ago, a miscarriage at four and one-half months six years ago and a cholecystectomy three years ago. She has had amenorrhea since the last miscarriage six years ago. In 1937 she received two roentgen treatments over the pituitary followed by two regular menstrual periods. Physical examination revealed no abnormalities of the heart, the pulse is 80 and blood pressure 110 systolic, 65 diastolic. The abdomen shows the scar over the gallbladder area and midline below the umbilicus. The uterus is small but palpable. What procedure can be followed?

M.D., New Jersey.

ANSWER.—Unless the young woman is desirous of having children there is no reason to try to induce uterine bleeding. However, if there is a psychic disturbance because of the absence of menstruation, bleeding may be induced by so-called withdrawal therapy. A simple way to accomplish this is to administer 10,000 international units of estrone hypodermically three times a week for two weeks. Usually bleeding occurs about eight or ten days after the last injection. However, this form of therapy will produce only one bleeding episode. If the physician desires to produce cyclic bleeding he will have to repeat the series of injections every month.

If the patient is anxious to have a baby it is essential to find out whether the ovaries are functioning. Two things must be done. One is to obtain an endometrial biopsy at weekly intervals to see the type of endometrium which is present. If successive biopsies show a change from proliferative to secretory endometrium, this is evidence of the presence of ovulation. It is possible to have ovulation without menstruation and vice versa. If biopsies reveal secretory endometrium there is no need to give the patient treatment for the amenorrhea. Since she ovulates she can conceive.

If, on the other hand, the biopsies show persistent proliferative endometrium or hyperplasia the patient does not ovulate. In addition to endometrial biopsies a study of the urine should be made to determine the amount of gonadotropic hormone. If there is an excessive amount of this hormone it indicates that the ovaries are not functioning properly. An attempt may be made to stimulate ovulation by the administration of the gonadotropic substance obtained from pregnant mares' serum but the results have not been encouraging.

The amenorrhea may be overcome by radiation therapy of the pituitary gland. However, this treatment should be carried out only by a skilful roentgenologist.

The patient should have a basal metabolism study. If the rate is low, thyroid medication should be given, because not infrequently thyroid extract overcomes amenorrhea in women with hypothyroidism.

UNUSUAL PAIN AT CLOSE OF MENSTRUAL PERIOD

To the Editor:—A woman aged 21 with no physical defects and a perfectly normal menstrual history has severe pains starting at the end of each menstrual period. These pains are of the same type as tic douloureux; that is, a severe pain comes on lasting two minutes with complete relief for six or eight minutes, only to be repeated. They increase in severity until she is given a hypodermic of morphine one fourth grain (0.016 Gm.). The pain is to the right of the median line, apparently over the right ovary. There is absolutely no tenderness on deep pressure. Ordinary analgesics have no effect. The condition has been going on for years. No pelvic examination has been made. Can you give me any enlightenment on this case?

L. C. Howe, M.D., Muscatine, Iowa.

ANSWER.—This is a puzzling type of pain for which there does not seem to be any physiologic reason. Therefore it is difficult to recommend any therapy. Endocrine treatment will almost certainly be of no avail. If the patient is a virgin, a bimanual recto-abdominal examination should be made to rule out a possible pelvic lesion. Otherwise a vaginal examination should be made. If no abnormality is found, a pelvic sympathectomy may be justified because of the long duration of the pain and because of the strong likelihood of making the patient a morphine addict.

LATE FALL ASTHMA

To the Editor:—A woman, aged 26, living in mideastern Wisconsin, complains of asthma-like attacks of many years' duration. She states that the attacks start in the latter part of September. The condition is at its worst late in October. "As soon as the leaves are off the trees," as the patient states it, she feels all right. Please advise me what kind of agent could cause these attacks of asthma or hay fever. The physical examination revealed wheezing all over her chest.

M.D., Wisconsin.

ANSWER.—It is not uncommon to find patients who have asthma after the ragweed hay fever season is over. At this season one must think especially of corn smut or corn dust and of molds; perhaps the asthma coincides with fall house cleaning and the patient may be sensitive to house dust. Perhaps the patient may be allergic to fruits which are being preserved or she may be sensitive to foods eaten particularly at this season, e. g. grapes, pumpkin, plums and pears. It may be too that the dog or cat is invited into the house as cold weather sets in. In most cases careful history and thorough skin testing, both cutaneously and intracutaneously, will reveal sensitivity to one or more antigens.

ADDICTION TO AMPHETAMINE (BENZEDRINE) SULFATE

To the Editor:—I wish to add my comments to the case reported on addiction to amphetamine (benzedrine) sulfate by Dr. L. J. Hahne in Queries and Minor Notes, November 2. First, his case is exceptional. I have used amphetamine (benzedrine) sulfate regularly in the treatment of alcoholism. I have run across no case in which the individual did not easily drop the drug after the desired results of prolonged abstinence from alcohol had been reached. The reason there have been no specific reports of cases of addiction to amphetamine sulfate is a simple one. Practically speaking, there are no such cases. In a continuous experience with the drug over the past four years I have not had one case which could be properly classified as drug addiction. True, there have been people who have suffered from chronic depression to whom the drug gave some degree of relief, who have continually used it during the period of time of treatment. However, they have not found it necessary to increase the dose in order to obtain the desired effect and, in fact, in the majority of cases the dosage has rarely been more than from one to one and one-half tablets a day, and in a considerable number of cases less than 10 mg. or one tablet a day has been sufficient. The psychologic effect is obtained more readily, I believe, with the smaller dose than the larger one. One might as well speak of the continued use of insulin by a diabetic patient as drug addiction. During the period of diabetes he has to take insulin steadily and continuously. When his disease recedes, so that diet alone is sufficient, he does not take insulin. The same situation prevails in the vast, almost overwhelming, majority of persons using amphetamine sulfate. Cases of sudden death have been recorded following the use of this drug but not beyond the range of mere coincidence. You cannot use any drug, including sterile saline solution, in a large number of cases without sudden death following an injection. If enough people with chronic or severe illness are treated with anything, death will ensue in some coincidental relationship. It is true that the drug should not be used when there is hypertension, gastrointestinal atony or profound excitement. Its use should be dropped immediately when good results do not follow quickly. Taking its total physiologic reactions into account and comparing it with other potent drugs, such as strychnine, atropine and digitalis, amphetamine sulfate is a relatively safe drug to use.

Abraham Myerson, M.D., Boston State Hospital, Dorchester Center, Mass.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS
EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, December 14, page 2107.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 17-19. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ARIZONA: * Phoenix, Jan. 7. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: * *Eclectic.* Little Rock, June 5-6. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, Jan 29. *Written.* Los Angeles, Feb. 24-27. Sec., Dr. Charles B. Pinkham, 1020 N St., Sacramento.

COLORADO: * Denver, Jan. 7-10. Applications must be on file not later than Dec. 23. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: * *Medical. Written.* Hartford, March 11-12. *Endorsement.* Hartford, March 25. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Homeopathic.* Derby, March 11-12. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: July 8-10. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * Washington, May 12-13. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: * Jacksonville, June 23-24. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, June. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Jan. 8-11. Sec., Dr. James A. Morgan, 48 Young Building, Honolulu.

IDAHO: Boise, April 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 335 State Capitol Bldg., Boise.

ILLINOIS: *Written.* Chicago, Jan. 21-22. *Reciprocity.* Chicago, Jan. 23. Supt. of Registration, Dept. of Registration and Education, Mr. Lucien A. File, Springfield.

INDIANA: Indianapolis, June 17-19. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, Citizens Trust Bldg., Fort Wayne.

MAINE: Portland, March 11-12. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MASSACHUSETTS: Boston, March 11-13. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN: * Ann Arbor and Detroit, June 11-13. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: * Minneapolis, Jan. 21-23. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: *Reciprocity.* Helena, March 31. *Written.* Helena, April 1. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEVADA: *Reciprocity with oral examination,* Feb. 3. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW HAMPSHIRE: Concord, March 13-14. Sec., Board of Registration in Medicine, Dr. T. P. Burroughs, State House, Concord.

NEW JERSEY: Trenton, June 17-18. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 14-15. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 27-30. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, State Education Department, 315 Education Bldg., Albany.

NORTH DAKOTA: Grand Forks, Jan. 7-10. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OREGON: * Portland, Jan. 14-16. Exec. Sec., Miss Lorienne M. Conlee, 608 Failing Bldg., Portland.

PENNSYLVANIA: Philadelphia, January 7-11. Acting Sec., Bureau of Professional Licensing, Miss Marguerite G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, Jan. 2-3. Sec., Division of Examiners, Dr. Robert M. Lord, 366 State Office Bldg., Providence

SOUTH DAKOTA: * Pierre, Jan. 21-22. Dir., Medical Licensure, Dr. J. F. D. Cook, Pierre.

VERMONT: Burlington, Feb. 11. Sec., Dr. W. Scott Nay, Underhill.

WASHINGTON: * Seattle, Jan. 13-15. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

WEST VIRGINIA: Charleston, March 3. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: * Madison, Jan. 14-16. Applications must be on file not later than Jan. 2. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

WYOMING: Cheyenne, Feb. 3-4. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT: Feb. 8. Address State Board of Healing Arts, 1945 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, April 21-22. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: De Land, June 7. *Applications must be on file not later than May 24.* Sec., Prof. J. F. Conn, John B. Stetson University, De Land.

IOWA: Des Moines, Jan. 14. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor, Detroit and East Lansing, Feb. 14-15. Sec., Miss Flora E. Dube, East Lansing.

MINNESOTA: Minneapolis, Jan. 7-8. Sec., Dr. J. Charnley McKinley, University of Minnesota, 126 Millard Hall, Minneapolis.

NEBRASKA: Omaha, Jan. 14-15. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

OREGON: Portland, Feb. 15. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

RHODE ISLAND: Providence, Feb. 19. Sec., Division of Examiners, Rev. Nicholas H. Serroe, Providence College, Providence.

WASHINGTON: Seattle, Jan. 9-10. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

Oregon June Report

Miss Lorienne M. Conlee, executive secretary, Oregon State Board of Medical Examiners, reports the written examination for medical licensure held at Portland, June 18-20, 1940. The examination covered 11 subjects and included 80 questions. An average of 75 per cent was required to pass. Thirty-one candidates were examined, all of whom passed. Four physicians were licensed to practice medicine by reciprocity and 3 physicians so licensed by endorsement. The following schools were represented:

School	PASSED Year Grad.	Per Cent
College of Medical Evangelists	(1940)	85.8, 89.1
Rush Medical College	(1939)	83, 92.1
State University of Iowa College of Medicine	(1939)	88.5
University of Louisville School of Medicine	(1939)	90.1
University of Minnesota Medical School	(1940)	82, 84.3
St. Louis University School of Medicine	(1939)	81.3, 83
University of Nebraska College of Medicine	(1939)	83.8
University of Oklahoma School of Medicine	(1939)	84.1, 86.9
University of Oregon Medical School	(1939)	80.9, 82.5, 84.4, 85.6, 85.8, 85.8, 85.9, 86.5, 86.6, 88.7, 89, 89.3, 89.9, 90.1, 90.6, 91.4, 91.5, 92.9

School	LICENSED BY RECIPROCITY Year Grad.	Reciprocity with
Detroit College of Medicine and Surgery	(1933)	Michigan
University of Oregon Medical School	(1938)	Minnesota, (1939) Wyoming
Osteopath *		Colorado

School	LICENSED BY ENDORSEMENT Year Grad.	Endorsement of
College of Medical Evangelists	(1940, 2)	N. B. M. Ex.
Harvard Medical School	(1938)	N. B. M. Ex.

* Licensed to practice surgery only.

West Virginia July Report

Dr. Arthur E. McClue, secretary, Public Health Council of West Virginia, reports the oral and written examination for medical licensure held at Huntington, July 1-3, 1940. The examination covered 11 subjects and included 110 questions. An average of 80 per cent was required to pass. Twenty-five candidates were examined, all of whom passed. Sixteen physicians were licensed to practice medicine by reciprocity and 1 physician so licensed by endorsement. The following schools were represented:

School	PASSED Year Grad.	Per Cent
College of Medical Evangelists	(1939)	85.9
Northwestern University Medical School	(1939)	88.7
Rush Medical College	(1937) 89.8, (1938)	87.1
University of Maryland School of Medicine and College of Physicians and Surgeons	(1939)	85.2, 86.5
Harvard Medical School	(1938)	87.9
St. Louis University School of Medicine	(1938)	87.6
Columbia University College of Physicians and Surgeons	(1935) 86.3, (1939)	86.3
University and Bellevue Hospital Medical College	(1901)	84.9
New York University College of Medicine	(1938)	88.5
Medico-Chirurgical College of Philadelphia	(1914)	86
Temple University School of Medicine	(1939)	86.5, 88.7
Medical College of Virginia	(1939)	85.1, 85.8, 87.1, 87.3, 87.5, 87.7, 87.9, 88.3
University of Virginia Department of Medicine	(1939)	85.3, 87.1

School	LICENSED BY RECIPROCITY Year Grad.	Reciprocity with
College of Medical Evangelists	(1934)	Maryland
University of Georgia School of Medicine	(1925)	Georgia
Northwestern University Medical School	(1925)	Indiana
Rush Medical College	(1937)	Minnesota
State University of Iowa College of Medicine	(1937)	Iowa
University of Louisville School of Medicine	(1937)	Kentucky
Wayne University College of Medicine	(1939)	Michigan
Long Island College of Medicine	(1936)	Dist. Colum.
Western Reserve University School of Medicine	(1936)	Ohio
Meharry Medical College	(1930)	Tennessee
Vanderbilt University School of Medicine	(1937)	Tennessee
Medical College of Virginia	(1927)	N. Carolina, (1937), (1939, 2) Virginia, (1939) Maryland

School	LICENSED BY ENDORSEMENT Year Grad.	Endorsement of
Temple University School of Medicine	(1935)	N. B. M. Ex.

Book Notices

Public Health Administration in the United States. By Wilson G. Smillie, A.B., M.D., Dr.P.H., Professor of Public Health and Preventive Medicine, Cornell University Medical College, New York City. Second edition. Cloth. Price, $3.75. Pp. 553, with 31 illustrations. New York: Macmillan Company, 1940.

Since the first edition of this book appeared five years ago there have been some extraordinary developments in public health administration in the United States. Some of these have been associated with new scientific information, such as that regarding scarlet fever, measles, influenza, the venereal diseases and particularly pneumonia. The relationship of nutrition to the public health has become more clearly defined, and the modern health department is greatly concerned with the general nutritional state of the people. The Social Security Act of 1935 revolutionized our national health program and modified greatly the administration of public health procedures. Dr. Smillie has reflected these changes in the new edition of his book, and he discusses the consolidation of the gains that have been made and the possibilities for the future. There is no longer any necessity for discussion as to the place of the public health officer in modern civic organization. However, the exact position which he is to occupy in relation to other phases of the public health is still a matter of considerable debate. It is well to find Smillie saying "The United States Department of Agriculture has estimated that one third of our population cannot afford to purchase even a minimum adequate diet. In our opinion this is a highly exaggerated statement." Of particular importance is a chapter on the practicing physician and the public health department. This material should be in the mind of every practitioner. A concluding chapter on the national health program discusses the present trend toward new legislation. Dr. Smillie is convinced that the United States is not ready for a nationwide plan of sickness insurance. He points out that we are not a totalitarian nation, that nationwide philosophies must develop slowly and must win the approval of the people who are to be benefited. Neither does he feel that our present organization of public health is ideal. Evolution is going on, and Dr. Smillie suspects that administrative devices which have not yet been initiated will eventually supplant our present type of organization.

Office Clinical Chemistry: A Laboratory Guide for the Practitioner and Hospital. By Emanuel M. Abrahamson, B.S., Ph.D., M.D., Adjunct Attending Physician, the Jewish Hospital of Brooklyn, Brooklyn. Cloth. Price $5. Pp. 245, with 39 illustrations. New York, Toronto & London: Oxford University Press, 1940.

This volume is designed to aid the clinician by selecting chemical methods for the examination of blood and urine which are suitable for office practice. It is not intended as a supplement or substitute for the existing treatises on laboratory procedures suitable to the large hospital laboratory with extensive equipment.

In general, the author has made an excellent selection of more than sixty established procedures adaptable for office practice. Many procedures have been modified so as to eliminate needless duplication of solutions of slightly different concentrations and apparatus of similar nature. A flow sheet of apparatus, reagents and order of procedure is graphically presented with each method in an attempt to simplify the technic. It is hoped that such an attempt at simplication will not mislead the clinician into the belief that preliminary training is not necessary in order to carry out accurately the various procedures. A knowledge of fundamentals is essential to recognize causes for inaccuracies.

While different workers in clinical laboratories may disagree with the author in certain of his selections and modifications of technics, it is obvious that in the main the selection has been wisely made with much thought toward simplification of procedures as far as is compatible with an accuracy sufficient for clinical interpretations.

To mention what might be regarded as a few deficiencies: The Kingsley method for albumin-globulin ratio is much simpler and more accurate than the one outlined. The newer sulfanilamide reagent N(1-naphthyl) ethylenediamine dihydrochloride gives a more rapid and stable color. Ordinary Exton's reagent for urinary albumin is generally used. Better calcium and phosphorus methods are available. Also, while ten pages is devoted to the Van Slyke apparatus for determining alkali reserve, followed by a note that the method is hardly suitable for office practice, a more simple and adequate titration method is not given. It would seem simpler also to purchase congo red paper and Nessler's solution. On page 41, in describing the preparation of protein-free blood filtrate, the author refers to the flask holding ten times the volume of blood. This would seem insufficient. To mention only one other impression: It would seem that the schema for determining the type of urinary calculus is unnecessarily involved, since the clinician usually desires to know only the type of calculus; that is, whether it belongs to the phosphatic, oxalic, uric or urate group or whether it is the cystine type, which occasionally is encountered.

This volume should serve a need that has long been felt by physicians in office practice and should be of great value to the clinician who desires to obtain clinical laboratory data in selected cases.

Principles of Animal Biology. By Lancelot Hogben, F.R.S., Regius Professor of Natural History in the University of Aberdeen, Aberdeen. Cloth. Price, $3.75. Pp. 415, with 151 illustrations by J. F. Horrabin. New York: W. W. Norton & Company, Inc., 1940.

This book, by the author of "Mathematics for the Million," lies somewhere between the semipopular book on science and the high school or college textbook. Its reading would be hard going for the average individual untrained in science and yet it is probably not complete or technical enough to serve as a textbook for a formal course although it would be excellent as collateral reading. There are a few errors: The sketch titled the human forearm shows the upper arm instead and is not good at that; the term ergosterol is twice mispelled; the statement that "an adequate minimum (vitamin A or carotin) seems to help resistance to diseases like colds and influenza" is not really warranted. Likewise the statement "The composition of what is now called vitamin E, present in cereal oils and green leaves, especially lettuce, is not yet known" scarcely does justice to the close approach which has been made to accurate knowledge of the structure of this vitamin. Also it would have been well if the statement that complete absence of this vitamin results in sterility from degeneration of testes in the male and resorption of early embryos in the female had been qualified by indicating that this result has been proved only in experimental rats.

The author has compressed a large amount of valuable information on science and has in the main expressed this information clearly. Nevertheless it does not seem to be a popularization that is likely to receive an extensive circulation nor is it quite suitable as a textbook. Perhaps its usefulness in future editions might be increased by some further thought on which of these purposes the book is designed to serve.

A Textbook of Medicine. By American Authors. Edited by Russell L. Cecil, A.B., M.D., Sc.D., Professor of Clinical Medicine, Cornell University Medical College, New York. Associate Editor for Diseases of the Nervous System: Foster Kennedy, M.D., F.R.S.E., Professor of Clinical Neurology, Cornell University Medical College, New York. Fifth edition. Cloth. Price, $9.50. Pp. 1,744, with 173 illustrations. Philadelphia & London: W. B. Saunders Company, 1940.

Textbooks of medicine increase in size continuously with the advancement of medical knowledge. Thus the present edition of Cecil's Textbook is 130 pages larger than the preceding edition. It appears with a green cover, whereas the previous edition was in blue. The book has been entirely revised and completely reset. One hundred and thirty-one additional illustrations are provided. Unfortunately, the paper used for a volume of this size makes reproduction of half-tone illustrations somewhat difficult, and the reproductions, particularly of x-ray films and of skin conditions, are not of the best. In the present edition there are new articles on equine encephalomyelitis, moniliasis, toxoplasmosis, disseminated lupus erythematosus, chronic bromide poisoning, riboflavin deficiency, uveoparotid fever, regional ileitis, amaurotic family idiocy and gargoylism. There are also new treatises on some of the topics previously covered as the result of the development of new information or the appearance of new research. Dr. Foster Kennedy, associate editor for diseases of the nervous system, has revised some of the chapters in that field. Recent advances in bacteriology have caused the transfer of Carrion's disease to the section on Rickettsial diseases and gangosa to the section on spirochetal infections. This one volume system on the practice of medicine

has earned for itself a high place in its field. The methods of presentation, the excellent editorship, the quality of the bibliography, the publisher's contribution, the excellent arrangement and the index assure for this work a position of leadership.

The Anatomy of the Female Pelvis. By F. A. Magulre, C.M.G., D.S.O., M.D. Third edition. Cloth. Price, 10s. 6d. Pp. 162, with 35 illustrations. Sydney & London: Angus & Robertson, 1940.

It is only forty years ago that we in this country drew rather steadily on British teachers in matters of obstetrics and anatomy and to some extent in gynecology. In their writings we looked for and we continue to look for clarity, sanity and vocabulary. Here we have a fair condensation of the subject, illustrated for the first time in the three editions. To these illustrations there are so many references that one is inclined to scrutinize them. Simplification that adequately depicts essentials is an achievement. In a few of the drawings, as in those of the lymphatics, this is the case, but where diagrams or near diagrams run to crude coarse lines they have little place, particularly with vulvas, where a measure of delicacy may be expected. Nor may a pelvic floor or a tube range twice the average thickness, nor a sacrum carry six sections throughout. Then again certain clinical points hardly fit American practice. A diagnosis of uterine position by the "impulse" rather than through routine bimanual palpation or seizure of the organ is one instance. Another is the repeated warning to take pains to avoid visualizing the vulva unless there is very positive evidence during the course of the examination that it needs inspection, thus setting us back to the early days of the pride in his skill of that doctor who always inserted the catheter under the darkness of the sheet —with the price in cystitis consequent on this modest achievement. This good summary from Australia needs all of it brought up to its best to compete with more successful textbooks.

Taber's Cyclopedic Medical Dictionary Including a Digest of Medical Subjects: Medicine, Surgery, Nursing, Dietetics, Physical Therapy. By Clarence Wilbur Taber and Associates. Fabrikold. Price, $2.50; Thumb-indexed, $3. Pp. 1,488, with 273 illustrations. Philadelphia: F. A. Davis Company, 1940.

This book represents an ambitious project as evidenced by the statement on the title page that it includes a digest of medical subjects—medicine, surgery, nursing, dietetics and physical therapy. It does actually contain an enormous amount of information of value to the medical man besides its service as a dictionary; for example, a table of the clinically significant blood constituents, their normal and pathologic ranges, and a list of phrases and words in four foreign languages devised particularly for assisting a physician in obtaining a history. The book also lists the etiology, symptomatology, physical signs and treatment of diseases. This has led, however, to what is probably the major criticism: The opening two sentences under "Treatment of Diabetes Mellitus," for example, are not wholly acceptable. They read "X-ray applied to the adrenals and pituitary glands is being tried, rather successfully. This relieves the necessity for frequent hypodermic injections of insulin." Similarly the treatment described for arthritis is not really illuminating. It is a doubtful contribution to the best medical interests to include such brief and in some instances distorted discussions of etiology, prevention and treatment of disease in a work of this kind. Nevertheless the amount of information contained in the book is amazing and it will serve as a ready source book for a good deal of miscellaneous information and as a satisfactory medical dictionary. The editor has obtained the help of an excellent group of associates.

A fonocardiografia. Pelo Dr. Dante Pazzanese, chefe do serviço de cardiologia do hospital municipal de São Paulo. Paper. Pp. 160, with 90 illustrations. São Paulo: Prefeitura do município de São Paulo, 1940.

The number of publications dedicated to the subject of phonocardiography is on a steady increase. They deal with the technic of recording, description of new apparatus or interpretation of tracings. In view of the growing interest of the medical profession in heart sound recording there is a need for a comprehensive monograph on this subject. Thanks to his extensive experience, the author was well qualified to fill this gap and he accomplished his task in an enviable manner. After a succinct discussion of the diagnostic and didactic value of phonocardiography and a brief historical review, he describes the most popular apparatus for heart sound recording and proceeds to analyze systematically the graphs in various cardiac lesions. Cambridge, Minot and Siemens recording apparatus were used by the author. To facilitate the interpretation of the tracings, simultaneous phlebograms or preferably electrocardiograms were made. There is no trace of loquacity, the style is simple, and reproductions of heart sound records are numerous and excellent. The book will prove invaluable to any physician interested in this newest method of examination of the heart.

Bibliography of Swimming. Compiled by Frances A. Greenwood, Department of Physical Education, University of Alabama, Tuscaloosa. Cloth. Price, $4.25. Pp. 308. New York: H. W. Wilson Company, 1940.

This bibliography is a comprehensive survey of the literature on swimming, beginning with a book published in 1538 and including about 10,000 titles classified under 600 subjects, which range from those directly connected with swimming itself to material on air conditioning, poetry, pools and bathing places, spas and mineral baths, and water softening. References of special medical interest are found under such headings as Corrective Swimming and Underwater Gymnastics, Cripples, Diseases and Infections, Drowning, Physiologic Aspects, and Resuscitation. Author and subject entries, arranged in the same alphabet, are made for each item listed, with complete bibliographic data under the author and English translations of foreign titles under the subject. As a whole, the material seems well organized with a helpful division into specific subject headings and ample cross references to guide the user.

A Research Conference on the Cause and Prevention of Dental Caries, Chicago, Illinois, July First and Second, 1938. Cloth. Price, $2. Pp. 178, with 4 illustrations. Chicago: The Good Teeth Council for Children, Inc., [n. d.].

This conference, held in July 1938, brought together representatives of eleven of the groups prominent in recent investigations in the field of dental caries from all over the United States and Canada. The proceedings contain not only the original papers but also a complete record of the discussion, which was both generous and critical. It therefore presents quite accurately the status of caries research as of July 1938 and, except for recent work in connection with fluorine and dental decay, gives a fair picture of the situation now, approximately two years later. It should be read not only by those who are interested or engaged in such research but also by all those who are concerned actively or otherwise in the prevention and about the cause of dental caries. It was truly characterized by one of the participants as "one of the most interesting presentations" ever listened to, but the original papers and discussions must be read and studied to be appreciated and evaluated. Even the closing summary by Dr. E. V. McCollum fails to develop the conclusions of the investigators and the results of the efforts through discussion to reconcile contradictions.

The Chronicle of Crichton Royal (1833-1936) Being the Story of a Famous Mental Hospital During Its First Century, and Illustrating the Evolution of the Hospital Care and Treatment of Mental Invalids in Scotland. By Charles Cromhall Easterbrook, M.A., M.D., F.R.C.P.E. With foreword: Some Early Crichton Memories, by the late Sir James Crichton-Browne, M.D., LL.D., F.R.S. Cloth. Price, 25s. Pp. 663, with 103 illustrations. Dumfries, Scotland: Courier Press, 1940.

The Crichton Royal Institution was founded in 1833 on an original estate of 40 acres (later increased to over 800) near Dumfries, Scotland, to care for mental invalids of all kinds. This book constitutes a review of the work of this institution over the intervening years, its staff, its physical additions and many other items of historical interest.

Psychiatry for Nurses. By Louis J. Karnosh, B.S., Sc.D., M.D., Associate Clinical Professor of Nervous Diseases, School of Medicine, Western Reserve University, Cleveland, and Edith B. Gage, R.N., Supervisor, Neuropsychiatric Division, City Hospital, Cleveland. Cloth. Price, $2.75. Pp. 327, with 34 illustrations. St. Louis: C. V. Mosby Company, 1940.

This book presents psychiatry "with an eye to the peculiar needs of the nursing school of today." In its twenty-nine brief chapters it offers first a historical review of the subject, then the structure and mechanism of the personality, taking up the classification of mental diseases and the examination and management of patients. More detailed consideration is given in later

chapters to the specific types of mental disease and to an outline of the various therapies now in vogue. The practical approach to the psychiatric patient is ably described and the theoretical aspects of psychiatry are brought into clear view. Brevity may account for certain omissions and may permit certain biased statements to creep in. For example, there is disapproval of psychoanalytic therapy without the credit given for the value of psychoanalysis as a key to psychiatric knowledge. Again, in the discussion on the treatment of epilepsy, large doses of bromides are featured without mention of acne and other complications. In the main, the authors have succeeded in preparing a readable book, brief, lucid and interesting. Questions at the end of each chapter, a glossary and an index add to its usefulness.

An Introduction to Pharmacology and Therapeutics. By J. A. Gunn, M.A., M.D., D.Sc., Professor of Therapeutics and Director of the Nuffield Institute for Medical Research, University of Oxford, Oxford. Sixth edition. Cloth. Price, $1.75; 6s. Pp. 242. New York & London: Oxford University Press, 1940.

Like its predecessors, the present edition of this well known little book provides the prospective student of pharmacology with a satisfactory didactic survey of the subject. The fact that six editions have appeared in ten years would seem to indicate that British students are well pleased with this method of approaching their course in experimental pharmacology. Doubtless the author requires supplementary reading of the more exhaustive textbooks in his own classes, as indeed he indicated in the preface to the first edition of this work; one would think, however, that there might be some danger of the lackadaisical type of student being satisfied with the preliminary sketch and never going on to a study of the larger canvas.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Libel: Publication Exposing Quackery Privileged Under State Statute.—In an article published in *Hygeia* entitled "Modern Medical Charlatans," the defendant, among other things, accused the plaintiff, John R. Brinkley, of being the apotheosis of quackery and of having made as much as $55,000 a week "from his various quackeries." The plaintiff later brought suit in the district court of the United States for the western district of Texas to recover actual and punitive damages for libel. The defendant pleaded the truth of the statements of fact in the article and that matters of opinion contained therein were based on facts and were his reasonable and honest opinions and so were privileged within the meaning of the Texas statute which declares that reasonable and fair comment or criticism of matters of public concern published for general information shall not be made the basis of an action for libel. The proceedings of the trial were published in J. A. M. A. **112**:1952 [May 13], 2050 [May 20], 2138 [May 27] and 2280 [June 3] 1939. Judgment was rendered for the defendant and the plaintiff appealed to the United States circuit court of appeals, fifth circuit.

Under the statutory law of Texas, said the circuit court of appeals, the truth of statements in publications is a defense to an action for libel even though the words are actionable per se. The testimony of the plaintiff tended to show the truth of the statements of fact complained of and there was no substantial evidence tending to show that the defendant was actuated by malice or that the plaintiff suffered any actual damage compensable in money. There remains to be considered, continued the court, but one more question—whether the expressions of opinion in the defendant's article were privileged under the laws of Texas. The gist of the defendant's article was that the plaintiff is a charlatan and a quack. According to the Century Dictionary, said the court, a "charlatan" is defined as "one who pretends to more knowledge or skill than he possesses, especially in medicine; a quack." A "quack" is defined as "an ignorant or fraudulent pretender to medical skill," and an element of quackery is "to advertise or urge, as a quack does his remedies." With respect to the plaintiff's professional qualifications and activities, continued the court, the admissions in his testimony tended to show:

> that he obtained his medical degree from an institution known as a diploma mill; that he had been practising medicine since 1915; that he began practising medicine in Milford, Kansas, in 1917; that he advertised, by pamphlets and newspapers and by radio broadcasting from his own station, an operation for transplanting goat glands in men for the purpose of sexual rejuvenation; that he had treated between 5,000 and 6,000 persons and he charged some of them nothing and some of them $750 for the operation; that his gross income was about $100,000 per month; that he abandoned this practice in 1933; that his license to practice medicine in Kansas was revoked in 1930 and his radio license was revoked by the Federal Communications Commission in 1930; that a license he had obtained to practice medicine in Connecticut was revoked; that he was indicted in California for a conspiracy to unlawfully practice medicine; that at the time the article was written he was advertising, by radio broadcasting from a Mexican station, his skill in treating prostatic troubles; that he would prescribe by letter for persons who wrote to him describing their symptoms, for which he charged $2.

All learned professions have their standards of ethics. A lawyer who advertises and gives advice by mail without seeing his client would certainly be considered a shyster. There was no doubt whatever that the plaintiff by his methods had violated accepted standards of medical ethics. In the judgment of the court, the facts quoted above were sufficient to support a reasonable and honest opinion that the plaintiff was a charlatan and a quack in the ordinary, well understood meaning of those words. The information contained in the defendant's article, concluded the court, was a matter of public concern and, since the article was published for general information, the published statements complained of were privileged. Accordingly the circuit court of appeals affirmed the judgment for the defendant. A petition by the plaintiff for a writ of certiorari was denied by the Supreme Court of the United States.—*Brinkley v. Fishbein, 110 F. (2d) 62; 61 Sup. Ct. 34.*

Libel: Baker Hospital Not a "Public Institution."—Defendant Norman Baker, the founder and owner of the Baker Hospital at Eureka Springs, Ark., in June 1939 wrote an open letter to Mr. and Mrs. Ray Freeman, residents of Eureka Springs, and to the Eureka Springs Boosters' Association and caused it to be published in a local newspaper, the *Daily Times Echo*. Mr. Freeman was a city official, a member of the Eureka Springs Boosters' Association and of the chamber of commerce and was financially interested in a wholesale grocery store, a swimming pool and a tourist camp. In this letter Baker used language tending to impeach the honesty, integrity, veracity and reputation of the Freemans. He accused them of making unfavorable comments about the Baker Hospital to persons who stopped at their tourist camp, persons who would otherwise have become patients of his hospital and would have spent a large amount of money in the city. He pointed out that all the local merchants would make more money if the Freemans desisted from actions which "are tearing down the good the Baker Hospital is doing." He said that the Freemans advised their patrons at the tourist camp to investigate about town before going to the Baker Hospital because it was a horrible and unfit place and had no licensed doctors. Finally he recommended that the boosters' association and the chamber of commerce expel Mr. Freeman from membership in their respective organizations and further that they sponsor a movement to oust or remove Mr. Freeman from city office. In conclusion he wrote:

> Can the citizens expect the Baker Hospital and other progressive citizens to give good co-operation as long as these ungentlemanly, underhanded and contemptible things exist?

On the basis of this letter, which the jury found contained false and untrue statements, the defendant was convicted of criminal libel in that he unlawfully, wilfully, maliciously and falsely exposed the Freemans to public hatred, contempt and ridicule. From this conviction Baker appealed to the Supreme Court of Arkansas.

Baker attempted to justify his remarks on the ground that the open letter was a privileged communication. His theory was that the Baker Hospital was a public establishment depending on the public for support and that therefore he had the right to defend that institution from unjust and malicious attack, as contained in false or untrue statements. The Supreme

Court, however, held that the Baker Hospital was not a "public institution" but was a purely private enterprise, and that it depended on public support only in the same manner and degree as does any other community enterprise, be it a department store, barber shop or meat market. There was nothing in the record to indicate that the Baker Hospital was an organized charity conducted in the public interest. Furthermore, said the court, in the first paragraph of the published letter the defendant assumed full responsibility for the statements contained therein and attempted to absolve the Baker Hospital from any blame that might follow from the publication when he stated: "It is understood that I write this personally, without any connection with the Baker Hospital, but as an honest and progressive citizen, interested in the welfare and upbuilding of the community." In the judgment of the court, this statement conclusively showed that the communication was not a privileged one and was not so regarded by the defendant himself. Accordingly, the Supreme Court of Arkansas affirmed the judgment of conviction of libel. Baker then petitioned for a writ of certiorari to the United States Supreme Court, but his petition was denied.—*Baker v. State (Ark.), 137 S. W. (2d) 938; 61 Sup. Ct. 25.*

Society Proceedings

COMING MEETINGS

American Student Health Association, Ann Arbor, Mich., Dec. 27-28. Dr. Ralph I. Canuteson, University of Kansas, Lawrence, Kan., Secretary.

Annual Congress on Industrial Health, Chicago, Jan. 13-15. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Philadelphia, Jan. 10. Dr. N. S. Weinberger, Robert Packer Hospital, Sayre, Pa., Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Chicago, Jan. 27. Dr. Walter H. Theobald, 307 North Michigan Blvd., Chicago, Chairman.

Society of American Bacteriologists, St. Louis, Dec. 27-29. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.

Society of Surgeons of New Jersey, Newark, Jan. 29. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.

Southern Section, American Laryngological, Rhinological and Otological Society, Nashville, Tenn., Jan. 8. Dr. William G. Kennon, Doctors Bldg., Nashville, Tenn., Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, San Francisco, Feb. 1-2. Dr. Robert C. Martin, 384 Post St., San Francisco, Chairman.

THE AMERICAN RHEUMATISM ASSOCIATION

Seventh Annual Meeting, held in New York, June 10, 1940

DR. LORING T. SWAIM, Boston, Secretary

(Concluded from page 2116)

An Oft Recurring Disease of Joints (Arthritis, Periarthritis, Para-Arthritis) Apparently Producing No Articular Residues

DR. PHILIP S. HENCH, Rochester, Minn.: The outstanding features of an unusual articular disease are multiple afebrile attacks of acute arthritis and periarthritis, sometimes also paraarthritis, with pain, swelling, redness and disability generally of only one but sometimes of more than one small or large joint of adults of either sex. The attacks appear suddenly, develop rapidly, generally last only a few hours or days and then disappear completely, only to recur at short or long irregularly spaced intervals. Despite the (transitory) presence of an acute or subacute inflammatory reaction in joint tissues and a fibrinopurulent exudate in the articular cavity (in some cases) there is little or no constitutional reaction or abnormality in laboratory tests, and no significant functional, pathologic or roentgenographic residues occur even after years of disease and scores or even hundreds of attacks.

Of the thirty-four patients nineteen were females, fifteen males. At the onset of the disease the patients were from 13 to 68 years of age (70 per cent were from 20 to 39). The disease had lasted from three months to twenty-five years, a total of 242 (average seven) years. Attacks had occurred at the rate of from two to ten yearly in nine cases, from twenty to sixty a year in seventeen cases, from 100 to 200 a year in three cases, and 250 or more a year in five cases; in the latter cases some joint or other was involved almost daily in a short attack, but successive attacks were not necessarily in the same joint. Four patients had each had "hundreds" of attacks; the remaining thirty patients had had a total of at least 4,930 attacks, an average of at least 164 attacks per patient within the average of seven years of illness, or twenty-three attacks per patient yearly.

The attacks lasted usually from one to three days, rarely more than one week. The intervals between attacks varied from only one or two days in those most frequently affected to one or six months in others. In 90 per cent of cases attacks were usually monarticular; occasionally two or more joints were simultaneously involved. Favorite sites were a finger joint, wrist, shoulder, knee, toe or elbow but practically any joint was liable to attack. Attacks appeared suddenly and progressed rapidly. Pain was sometimes mild, generally a severe ache, occasionally severe enough to require narcotics. Disability was considerable, producing temporary loss of function of the affected joint. Some patients were often forced to go to bed.

Red, tender, painful para-articular swellings occasionally appeared in 30 per cent of the cases at characteristic sites; they lasted only six to twenty-four hours; they differed from angioneurotic edema. In three cases intracutaneous or subcutaneous nodules also occurred occasionally, generally on the fingers.

There was little or no constitutional reaction, no fever in any attacks observed, no loss of appetite, generally no weight loss. Anemia was absent in 94 per cent. Total white counts were generally normal, but a relative lymphocytosis without eosinophilia was generally present. Sedimentation rates were generally normal between attacks and generally but not always slightly elevated during attacks (the average of thirty-three tests was 24 mm.). A moderate lipemia was present. Of the 164 roentgenograms of joints made, 150 (91 per cent) were entirely negative; the rest revealed coincident unrelated disease (bunions, hypertrophic changes in elderly patients).

Biopsies made during attacks (three cases) revealed an acute or subacute inflammation in synovial membrane and capsule, sometimes in tendon sheaths, and a fibrinopurulent exudate in the joint cavity. A biopsy of a knee between attacks revealed no gross or microscopic abnormalities.

The cause of the disease was not determined. The evidence collected against an allergic hypothesis outweighed that for it. Cultures of biopsy material were negative. Differentiation of this condition from atrophic arthritis, intermittent hydrarthrosis and gout was made. The cases possessed many of the features of the "angioneural arthrosis (periarthrosis, parathyrosis)" of Solis-Cohen (1913) or of Kahlmeter's (1939) "allergic articular and periarticular rheumatism," but certain differences were described.

Treatment included epinephrine, ephedrine, benzedrine, ergotamine tartrate, removal of foci, autogenous vaccines, low purine diets, diets free of suspected foods, histaminase, histamine desensitization and typhoid vaccine reactions. None of these methods gave impressive results. Follow-up data on twenty-seven cases were reported. A cure (spontaneous?) had occurred in four cases (15 per cent), slight improvement in twelve cases (44 per cent) and no change in seven cases (27 per cent); three patients (11 per cent) were having more frequent (but not longer) attacks. One patient died of coronary disease. There appeared to be no tendency for the disease to become chronic in a given joint. Despite the thousands of attacks suffered during a grand total of 307 years of illness (242 prior to plus sixty-five years since admission) no permanent crippling had affected any joint.

DISCUSSION

DR. K. K. SHERWOOD, Seattle: No matter how detailed and clearcut the description of a syndrome of arthritis is, it warrants reemphasis that this syndrome portrays a variant from the ordinary forms of chronic infectious arthritis both as to etiology and as to cause and is not a new disease but a variation. With this reservation I feel that the splitting of chronic arthritis not only into the hypertrophic and atrophic group but into smaller

subdivisions of clinical syndromes is of great value prognostically and therapeutically. This description may be held as a classic example of how each individual syndrome of chronic arthritis should be described and isolated if it is to be considered as a variant. Several years ago Dr. Hench described the occasional startling remissions occurring in chronic infectious arthritis with the onset of jaundice. Essentially each of these attacks resembled a case of chronic infectious arthritis of hours' duration rather than of months' duration. I have observed early cases of atrophic arthritis in which the joint symptoms preceded the constitutional manifestations of the disease and feel, therefore, that this syndrome might be regarded as an abortive form of true infectious or atrophic arthritis. It would seem worthy of detailed investigation in the cases described by Dr. Hench to determine whether or not a factor of abnormal liver metabolism might not be the reason for the nonprogression of these cases. A detailed study of the liver function in these cases might be of value in aiding one in learning why jaundice occasionally is of such dramatic therapeutic value.

DR. RUSSELL L. CECIL, New York: I cannot recall having seen a case exactly like the cases described, though I am sure we have all had the experience from time to time of seeing cases of joint swelling which we could not classify. I recall several in which I suspected an angioneurotic phenomenon. I am not referring to classic intermittent hydrops. I have seen several of the latter develop typical rheumatoid arthritis. Dr. Hench's cases should not be confused with intermittent hydrops, and the disease should not be called rheumatoid arthritis because of the lack of constitutional reaction and the failure of the disease to make any permanent changes in the joint. There is no progress toward chronicity and no injury to the synovial membrane. It seems that Solis-Cohen looked on this condition as an angioneurotic phenomenon, while Kahlmeter leaned more toward the allergic point of view. Dr. Hench has shown in his pictures that an actual leukocytic exudate was present in more than one case. It would hardly be fair, therefore, to call such a condition a purely angioneurotic state. I believe that the hypersensitive joint is something we are just beginning to understand.

DR. RALPH K. GHORMLEY, Rochester, Minn.: It has been my privilege to see a few of these patients from time to time with Dr. Hench, and I wish to corroborate as far as I am able the statements he has made and the facts he has presented, particularly as far as the pathologic changes are concerned. I have examined these tissues and they do not present a picture of infectious arthritis. The leukocytic exudation is more striking in some of the specimens than in those he showed on the screen.

DR. WALTER BAUER, Boston: It is too soon to say that the thirty-four patients described by Dr. Hench are suffering from one and the same disease. I myself believe that follow-up studies will show that he has included a number of diseases. On the other hand, it must be realized that from 5,000 to 6,000 cases of joint diseases are seen at the Mayo Clinic each year. Therefore it is conceivable that he has gradually weeded out thirty-four patients suffering from a rare disease or syndrome. His figures are not as impressive as they would appear at first glance, 642 years of the disease without any residual of joint changes. If one scrutinizes his analysis, one finds that five patients had the disease less than one year and another ten less than five years. I believe it is impossible to say what these fifteen patients are suffering from. The pathologic changes described could fit any number of acute diseases involving articular tissue. Oft repeated sedimentation rates, leukocyte counts and rectal temperatures on all these patients would be of considerable diagnostic help. One must further realize that diseases may vary considerably in clinical pattern. The same disease in one patient may be extremely atypical and benign, and in another individual it may have a malignant course. This group may have included atypical examples of rheumatic fever, rheumatoid arthritis, gout and allergic diseases.

DR. J. ALBERT KEY, St. Louis: I think this is definitely a disease syndrome. One cannot expect them all to last fourteen years. I should like to know whether there was any preponderance of eosinophils in the sections. Any acute reaction that lasts a few days will give a polymorphonuclear leukocytic exudate. I have seen one or two and thought they were allergic. They do resemble an abortive gout.

DR. PHILIP S. HENCH, Rochester, Minn.: There was no notable increase of eosinophils either in the circulating blood or in the sections of inflamed tissue removed for biopsy. When I use the term "new syndrome" I refer to one which is new to the consciousness of the general practitioner and even to the "rheumatism specialists" of today. The disease, of course, is not new, and Solis-Cohen and Kahlmeter may indeed have described the same disease. In describing a new syndrome it is difficult not to adulterate the series with cases which do not belong to it. It is therefore natural to suggest that I have fallen into such an error and included cases which in time will be recognized as somewhat atypical rheumatoid arthritis or rheumatic fever. However, I feel that I have already excluded such cases; I discarded a few cases that at first resembled those of the series in some degree but in which within a few months to two or three years the patients began to have longer and longer attacks, which finally became continuous. But there remains a group of thirty-four patients observed over a total period of 307 years, almost ten years each, who present the characteristic and unusual clinical picture which I have described. Do we have the right to consider them to have atypical atrophic arthritis and then wait for the permanent residual intra-articular changes of atrophic arthritis to show themselves? We must be open minded; we must not give a new name to every variety of one disease, but at the same time we must be ready to recognize a new syndrome when faced with it clearly and repeatedly. However, three of these patients were physicians, one a distinguished orthopedic surgeon. Having studied their own disease long and intensively, to them the diagnosis of atrophic arthritis or any other recognized syndrome had long since become quite untenable. We are now seeing seven to nine cases a year and the condition may be commoner than is now apparent. We shall certainly follow our cases closely and I hope to report again concerning them at a later date.

The End Results of Synovectomy of the Knee Joint

DRS. R. K. GHORMLEY and D. M. CAMERON, Rochester, Minn.: A review of the end results in cases in which synovectomy has been performed at the Mayo Clinic reveals the fact that synovectomy has been performed 103 times on eighty-eight patients. Of these, fourteen underwent bilateral synovectomy and one underwent synovectomy of an ankle in addition to synovectomy of both knees. Without resorting to argument as to the feasibility of synovectomy for other joints, we believe that it is a procedure most adaptable to the knee joint, and that other joints can be left out of consideration in this abstract. The operations were performed for chronic synovitis, chronic infectious arthritis, traumatic arthritis, synovial osteochondromatosis, xanthoma of the synovial membrane, intermittent hydrops, tuberculosis, hypertrophic arthritis and chronic synovitis which later developed into polyarthritic involvement, but which in all probability was chronic infectious arthritis at the onset. Of the patients undergoing this operation, end result studies show that three are dead (one from operative shock), and the end results are known in ninety cases in which operation was performed. Of the ninety patients, 34.4 per cent are in excellent condition, 33.3 per cent are improved, and 32.2 per cent are in poor condition, at the time of writing. Studying the end results by groupings, it is found that all the patients with traumatic arthritis, osteochondromatosis, xanthoma and hypertrophic arthritis were either cured or improved. Of the patients who had chronic synovitis, 77.4 per cent were cured or improved, whereas 56.2 per cent of those who had chronic infectious arthritis were improved or cured and 54.9 per cent of those who had synovitis which later developed into chronic infectious arthritis were improved or cured.

DISCUSSION

DR. PAUL P. SWETT, Bloomfield, Conn.: By a slight rearrangement of the figures it is found that out of fifty-two cases of atrophic arthritis only twenty-four showed a combination of improved or excellent results. Thus the authors' figure of about 50 per cent improvement agrees with Dr. Inge's recently reported conclusion that synovectomy offers a chance of helping about

half of the cases of atrophic arthritis. This means that we are not yet able, after neatly twenty years' experience, to define the conditions under which synovectomy can be expected to yield a high percentage of good results. This is especially unfortunate because it is highly important to be able to give exact indications for any operation which might add to our resources for managing the great group of the chronic arthritides which is most in need of treatment and in which synovectomy sometimes yields brilliant results. To clarify this situation it may be said that the successful use of synovectomy must be based first on consideration of the type of the disease and second on the stage of the process. Under the type of the disease it must be remembered (1) that the operation is applicable only to a synovial proliferative process, (2) that, as was first shown by Nichols and Richardson and later confirmed by Allison and Ghormley, the characteristic pathologic change in atrophic arthritis is proliferation but, while this commonly first occurs in the synovia, it also occurs in the perichondrium, the endosteum and the epiphysial connective tissue and (3) that, as has been emphasized by Pemberton and Osgood, there are two important variants of the disease in which either capsular fibrosis or muscular fibrosis is the predominant characteristic. Hence in the selection of the candidates for synovectomy it is necessary to exclude those cases in which the proliferative process is not primarily and predominantly synovial as well as those variant types which obviously are not suitable for this form of treatment. The stage of the process in which synovectomy may be most useful is (1) as soon as it can reasonably be determined that the proliferation is not going to undergo spontaneous resolution, (2) before the proliferation has caused irrevocable damage to the joint structures and (3) before protracted invalidism has so depleted the patient that no form of treatment can any longer be helpful. It is probable that the failures of synovectomy are to be found among those cases in which the disease was not primarily and predominantly synovial or in those instances in which the operation was done too late. Further reports on this work should be based on a series of observations in which the conditions outlined have been fulfilled.

DR. FRANK D. DICKSON, Kansas City, Mo.: It has been my experience over the last twenty years in some 140 synovectomies that proper removal of the synovia and other material in an infected joint results in a large percentage of cases in improvement in other joints. It is something that happens far too often in my exerience to be ignored. I believe that many failures in synovectomy are traceable to an incomplete operation. If one simply removes the synovia and leaves behind disintegrated semilunar cartilages and joint cartilage which is partly or largely destroyed by pannus, and projecting hypertrophic margins, one cannot expect a good result. Synovectomy to be successful must be complete, and this in the knee always includes removal of the semilunar cartilages, removal of all cartilage destroyed or partly destroyed by pannus, removal of all hypertrophic osteophytes, and reducing the joint surface to an area represented by the cartilage which was considered satisfactory enough to be allowed to remain in place. If more thorough, more complete, operations were done the results would be better. Only a few months ago I did a complete synovectomy on a right knee and a partial one on the left. The patient came back after two months with the right knee in excellent condition but the left knee about as bad as it had been before. I then operated on the left knee again and did what ought to have been done in the first place, a complete synovectomy, with later a satisfactory result on the left knee also. I believe the result obtained by synovectomy is entirely dependent on the thoroughness of the operation performed.

DR. J. ALBERT KEY, St. Louis: I have seen some of Dr. Dickson's cases and I am convinced that he is right. By doing a radical synovectomy in some of these early cases of presumable rheumatoid arthritis in which the principal disease is in one or both knee joints, his results are good. In intermittent hydrarthrosis this is the operation of choice even though it does not always cure.

DR. RALPH K. GHORMLEY, Rochester, Minn.: I agree with Dr. Swett that the selection of the cases is the important thing. We have tried to select cases only when the synovial membrane was involved and the articular surfaces were intact. Dr. Dickson's cases were more advanced. It seemed to me that he has opened up a further indication for this operation by doing a more complete operation. It is helpful to put on casts for ten days and then start movement—passive movement at first, then later active movement. Later, manipulation for three or four weeks may be helpful.

Experiences with Roentgen Therapy in Various Rheumatic Conditions

DRS. C. J. SMYTH, R. H. FREYBERG and W. S. PECK, Ann Arbor, Mich.: One hundred patients, the majority of whom had characteristic rheumatoid arthritis, others having rhizomelic spondylitis, degenerative joint disease or so-called fibrositis, were given roentgen therapy to some of the joints. For the most part, patients were selected having pairs of comparably affected joints and in such cases roentgen treatment was applied to only one of the pair, the other untreated joint serving as a control. In still other cases the possible psychic effect of such treatment was studied by screening some joints with lead so that no x-rays reached the skin. The effect of such treatment was measured by careful study of the subjective response, physical changes at the joints, frequent erythrocyte sedimentation rate determinations, diagnostic x-ray examinations of the joints, changes in joint fluid from both treated and untreated joints before and after roentgen therapy and in several cases by microscopic study of joint capsule and synovial biopsies. The results of treatment are analyzed in regard to the type of disease, the duration of illness, activity and extent of the disease.

DISCUSSION

DR. W. PAUL HOLBROOK, Tucson, Ariz.: Last year Dr. Freyberg discussed sulfur therapy and buried it thoroughly. This year it is roentgen therapy. It will take Dr. Freyberg only a few years to dispose of all our therapeutic agents at the rate he is going. This is a carefully controlled experiment with roentgen therapy. A few years ago Dr. Kahlmeter reported on the subject and I have done a little work with it. Dr. Kahlmeter's cases were certainly not controlled as Dr. Freyberg's have been. My experiences, though small, have been identical with those obtained by Dr. Freyberg in rheumatoid arthritis. I have experienced two differences. First I have had better luck in the control of pain about the shoulder from bursitis with roentgen treatment than Dr. Freyberg indicated. Whether it has anything to do with curing the disease or not I do not know, but if the pain can be controlled it is helpful. Second, I have had no such brilliant results with spondylitis as Dr. Freyberg reports.

DR. LORING T. SWAIN, Boston: This paper represents the beginning of the best controlled study of roentgen therapy to date. The estimate of the results in arthritis is difficult because of the nature of the disease and the psychologic effects of any and all forms of treatment. It is a purely local form of treatment and should not be expected to affect the constitutional disease. No changes have been found in the sedimentation rate; the x-rays cause no beneficial change in the bones or joints. I believe the effect is in the soft tissues and that they appeared gradually less swollen and that ultimately the growing villus tissue in the joints decreased. I believe the chief value is in decrease of pain due to hyperemia in the soft tissues. Spasm is consequently less and motion increases. My colleagues and I were not particularly impressed with the psychologic effect of roentgen treatment in our cases and therefore did not use a lead screen. This is a valuable addition to methods of control. We have treated one of two joints in many cases, but this does not give an adequate control of the mental factors. We have not stopped other treatments, but in certain cases merely added roentgen treatments.

Roentgen treatment was begun at the Robert B. Brigham Hospital in 1932 of one child whose left knee had been operated on for synovial overgrowth with poor results. X-rays have given her an excellent right knee, eight years later. Up to March 1940 we have completed treatment of 164 patients. Of these eighty-five were for rheumatoid arthritis, thirty-one for osteo-arthritis, twenty-eight for a combination of osteo-arthritis and rheumatoid arthritis and eighteen for Strümpell-Marie arthritis. Treatment was first given for relief of pain, but it

was soon observed that swelling and limitation of motion decreased gradually under roentgen treatment. We have listed the end results according to subjective improvement and objective improvement. By subjective improvement we mean relief of pain and stiffness. By objective improvement we have listed measurable decrease in swelling and measurable improvement in motion. There were no observable roentgenologic changes except that recalcification of the bone was observed somewhat more frequently in patients receiving roentgen treatment in comparison to those not receiving roentgen treatment; this has been mentioned in medical literature. No complications or untoward reactions were observed. In the patients with rheumatoid arthritis, subjective improvement was observed in over 90 per cent of those in whom the swelling and pain in the joints had been of six months duration or less. There was also objective improvement. Of the patients whose arthritis was from six months to two years in duration subjective improvement was observed in about 85 per cent and objective improvement in 60 per cent. Of the patients whose arthritis was of long duration, over two years, subjective improvement was observed in about 72 per cent and objective improvement in 52 per cent. Of the patients with osteo-arthritis there was no appreciable difference between the early, moderately advanced and late cases. These were improved subjectively in 70 per cent and objectively improved in 45 per cent. Of those patients who had evidence of both rheumatoid arthritis and osteo-arthritis there was subjective improvement in only 63 per cent and objective improvement in 25 per cent. In Strümpell-Marie arthritis relief of pain in the back was observed in only three cases. Pain in the hip or shoulder joint was relieved in 50 per cent of the patients; objective improvement was observed in about 15 per cent.

In rheumatoid arthritis, the earlier the case is treated the more rapid is the response. Children seem to respond more quickly to this form of treatment than adults. Frequent small doses continued for a long period of time give better results than larger doses given at longer intervals or for only a few times. In the Strümpell-Marie arthritis improvement was noticed only when twelve or more treatments had been given at fairly frequent intervals—two weeks or less. Improvement was usually observed only after the lapse of a year. Treatment was of three types: For small joints (knee joint or smaller) the following formula was used: 118 kilovolt peak, 5 milliamperes, 1 mm. of aluminum filter, 90 roentgens per minute, two and one-half min. = 225 roentgens, 14 inches distance. For spines, 130 kilovolt peak, 5 milliamperes, 3½ mm. of aluminum filter, 39 roentgens per minute, 5 minutes = 195 roentgens, 14 inches distance. For osteo-arthritis of the knees and hips, 130 kilovolt peak, 5 milliamperes, 3 mm. of aluminum filter, 39 roentgens per minute, 2¾ minutes = 107¼ roentgens, 14 inches distance. These formulas were gradually developed after several years of trial and seemed to be the best in our experience for the conditions listed. Treatments were given on the average of once every two weeks. The formula we believe is important.

I would ask Dr. Freyberg to reserve judgment about his results both objective and subjective until from three to five years has elapsed. Our belief is that early, adequate roentgen treatment of rheumatoid arthritis is helpful locally. It relieves pain in osteo-arthritis, and has helped hips in Strümpell-Marie spondylitis.

DR. EUGENE T. LEDDY, Rochester, Minn.: Most of the cases of arthritis referred to the radiologist for treatment are in the group for which little can be done, and one in which the results of treatment are in no sense outstanding. The technic of the roentgen treatment of arthritis is by no means standardized and is largely a matter of choice of the radiologist. Most of us have a few fairly definite rules which we modify to fit the individual case. My own view is that, since arthritis is a chronic inflammatory disease, the use of both high voltage and high doses is unnecessary. I therefore feel that the technic described by Dr. Freyberg is too intensive. In general, the earlier the stage of arthritis the better is the result, and I think that the more acute the case, the lower should be the dose of x-rays used in its treatment. There is one type of arthritis which I think is unfavorable for roentgen treatment, and that is the group in which there has been deposition of bone. I know of no radiologic technic which will cause dissolution of these bony deposits. However, roentgen treatment is worth a trial in this group for its possible pain-relieving effect. In many cases of arthritis, relief of pain follows roentgen treatment without there being any changes demonstrable in the roentgenogram to account for it. The explanation of the effect of roentgen treatment on arthritis is somewhat controversial, but I feel that it is largely destruction of leukocytes in the inflammatory process.

DR. ERNST FREUND, Boston: In rheumatoid arthritis as well as in other chronic diseases it is helpful to have a treatment which gives a symptomatic result. In some cases in which inflammation is present the results are better if one first removes the effusion by puncture or by physical or medical means. One of the first indications of periarticular disease is involvement of the shoulder, followed by the hip and knee. In some the results obtained by x-rays are better than with other means. I have never treated women between the ages of 15 and 45 with x-rays for sciatica or sacro-iliac arthritis because I have seen some treatment given elsewhere which resulted in sterility. Some other diseases, such as superficial irritations of the periosteum, like epicondylitis and styloiditis, and similar conditions such as bursitis, respond well to roentgen treatment. I have had relatively good results with this kind of treatment.

DR. JOSEPH A. FREIBERG, Cincinnati: I myself have seen no harmful effects of roentgen therapy but I do not think it should be given in this condition, especially since Dr. Freyberg mentioned that in several of his cases there was an increase in osteoporosis following therapy. Whether he attributed the osteoporosis to the therapy I was not quite certain. We attempt to increase the blood supply, and if high voltage roentgen therapy or any similar treatment is used we may lessen the blood supply to the joint subsequently. I do feel that roentgen therapy is used rather promiscuously in some instances about joints. I have seen extensive osteoporosis following high voltage therapy. I think it would be questionable to use roentgen therapy in arthritis unless it has some very definite effect which cannot be obtained by other means.

DR. R. H. FREYBERG, Ann Arbor, Mich.: I am not a therapeutic nihilist, but I do think that an appraisal of all forms of therapy should be made under controlled conditions and with no undue enthusiasm. Dr. Holbrook mentioned that the results of treatment of spondylitis in his group of patients had not been as brilliant as ours. I do not think our results should be considered brilliant. I contrasted them with results in patients with rheumatoid arthritis, among whom I think they were distinctly poor. We have been encouraged to continue to use roentgen therapy in spondylitis. Diagnosis in the earlier stage of rhizomelic spondylitis is difficult. It is obvious that late in the course of the disease one cannot expect cures from any therapy. If one is going to help these patients one must use treatment of value in the early stage. The patients in whom we observed the best results were those seen early in the stage of development of signs and symptoms characteristic of rhizomelic spondylitis; there was no demonstrable calcification of the paraspinous ligaments; the erythrocyte sedimentation rate was elevated. We have followed our patients, with few exceptions, for at least six months; 50 per cent were observed for more than twelve months, and many for more than eighteen months after treatment. We think this is long enough to get an idea of what effect x-rays will have. We have had no experience in treating younger individuals as Dr. Swaim has. Our patients have always been adults. The technic of irradiation may explain the results that Dr. Swaim mentioned in contrast to ours, though we think it quite unlikely. The development of technic in treatment of rheumatic diseases so far as I can find is about as mysterious as the use of it at all. Dr. Swaim's technic differs from ours in that treatment was given more often and for a longer period. Dr. Freund mentioned getting better results when synovial fluid was removed from the joints later treated. We have observed no difference in aspirated and unaspirated joints. I am glad Dr. Freiberg raised the question about the ill effects. We have had no ill effects except nausea and vomiting lasting for only a few days during treatment. Depilation and pigmentation of the skin occurred in some cases. We saw one patient treated elsewhere who had cutaneous changes indicative of a roentgen dermatitis. I want to add my warning that one should keep in mind the possible harmful effects.

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

20:389-518 (Oct.) 1940

Morphologic Study of Cardiac Conduction System in Ungulates, Dog and Man: Part I. Sino-Atrial Node. D. J. Glomset and Anna T. A. Glomset, Des Moines, Iowa.—p. 389.

Mechanism and Nature of Ventricular Fibrillation. C. J. Wiggers, Cleveland.—p. 399.

*Physiologic Basis for Cardiac Resuscitation from Ventricular Fibrillation: Method for Serial Defibrillation. C. J. Wiggers, Cleveland.—p. 413.

Estimation of Cardiopulmonary Functional Capacity by Means of Oxygen Debt Studies. F. C. Sutton, Cleveland; J. A. Britton, Chicago, and J. G. Carr, Evanston, Ill.—p. 423.

Combined Use of Ouabain and Digitalis in Treatment of Congestive Heart Failure. R. C. Batterman, O. A. Rose and A. C. DeGraff, New York.—p. 443.

*Rheumatic Heart Disease: Analysis of 796 Cases. B. J. Clawson, Minneapolis.—p. 454.

Diagnosis of Coronary Occlusion and Myocardial Infarction by Fluoroscopic Examination. A. M. Master, R. Gubner, S. Dack and H. L. Jaffe, New York.—p. 475.

Effects of Whole Bile and Bile Salts on Innervated and Denervated Heart. K. G. Wakim, H. E. Essex and F. C. Mann, Rochester, Minn. —p. 486.

Cardiac Resuscitation from Ventricular Fibrillation.—Wiggers points out that the high incidence of death from ventricular fibrillation secondary to coronary occlusion and accidental electrocution from electrical appliances make ventricular fibrillation of special interest. The author's experience has convinced him that the physiologic basis for resuscitation rests on the conception that ventricular fibrillation is not a constant phenomenon but an evoluting series of changes from the moment of its inception until its cessation, which consumes from thirty to forty-five minutes. Asynchronicity and incoordination involve progressively smaller blocks of myocardium, in which the character of the contraction alters as anoxia progresses because of the cessation of coronary flow. Consequently, restorative procedures must recognize the state which exists at the time the procedures are applied. For example, the atonic stage of fibrillation, in which anoxia causes depression of contractile force and slows conduction, develops in from two to five minutes after the onset of fibrillation. Although fibrillation can be readily stopped at this time, the coordinated beats which redevelop are exceedingly weak and dynamically useless. Consequently, one of the problems of revival consists in finding a means which can be employed within the first three minutes or in devising expedients for more forceful beats. The use of powerful stimulants, such as epinephrine and related substances, must necessarily prove valueless because they cannot substitute for oxygen lack. The author, as well as Wegria, has had success in his experimental work with a modification of the countershock method, which he calls serial defibrillation. The modification consists in applying to the ventricles, through padded electrodes, a series of brief and weaker alternating current shocks. Each shock lasts less than one second and has a strength of approximately 1 ampere; one or two seconds elapse between the shocks. As a rule, from three to seven shocks suffice. The effects are that each successive alternating current shock tends to merge smaller fibrillating areas into larger ones, until a convulsive state is redeveloped. A final shock stops the fibrillation and initiates coordinated beating by natural pacemakers. It is their impression that the deeper myocardium and septum are thus included in fibrillating circuits and, in consequence, these larger circuits are interrupted without the actual passage of currents through the deeper layers and septum. The likelihood of inducing auricular fibrillation is reduced. Since September 1939, out of 328 attempts the author and Wegria have had 327 revivals and they have succeeded forty-one times in one dog. The author suggests that studies be made on larger animals to ascertain whether weaker currents might not suffice if the method of serial defibrillation were used. The difficulties of meeting the conditions necessary for reviving human fibrillating hearts are analyzed and the conclusion is reached that, although such an achievement is not impossible, remarkable results in the present state of knowledge cannot be anticipated until further methodical research suggests a way of rendering the ventricles less sensitive or refractory to fibrillating agents.

Rheumatic Heart Disease.—Clawson states that if tuberculous pericarditis is excluded, heart failure caused by an adherent pericardium appears in most cases to be the result of rheumatic infection. The condition is seldom seen except in association with rheumatic valvular involvement. From 1910 to 1937, 27,957 necropsies were performed at the University of Minnesota, and 4,254 of these revealed noncongenital cardiac disease (15.2 per cent). In 1,598 (37.6 per cent) of these the disease was infectious in origin (rheumatic, bacterial, syphilitic, toxic myocarditis). There were 796 cases of rheumatic heart disease, comprising about 50 per cent of all cases of infectious heart disease and 18.7 per cent of the cases of noncongenital heart disease. He distinguishes four types of rheumatic heart disease: acute rheumatic endocarditis, recurrent rheumatic endocarditis, valvular deformities and adherent pericardium. The respective incidence of these four types was 12.3, 9.5, 73.5 and 4.52 per cent. Death from acute and recurrent rheumatic endocarditis occurred in the early decades, from incompletely or completely healed valvular deformities in the middle decades, and from the calcific, nodular, aortic valve deformity in the later decades. Death solely as a result of adherent pericardium is rare. The sex incidence was males 27 per thousand and females 31 per thousand. Female patients died earlier than the male patients, probably because in them the mitral valve is most commonly involved. The nature of the inflammatory reaction within the valve was similar to that of frank streptococcic subacute bacterial endocarditis. The valves of the left side of the heart were involved in 99.8 per cent of the patients. There was right-sided involvement in 5.6 per cent, but this was accompanied by a lesion of one or both valves of the left side. The aortic and mitral valves were involved with equal frequency in male subjects. The predilection for the mitral valve in female patients is not understood, but it helps to explain why calcified nodular aortic deformity is common in old men. Vegetations begin on the side of the valve where the spongiosa layer is located, suggesting that the infection may be embolic in origin. However, in some cases small vessels can be seen leading from surface indentations, indicating that infection may occur directly from the blood stream. Auricular endocardial involvement was almost as common in acute rheumatic endocarditis as in bacterial endocarditis. Hypertrophy was present in most of the cases. It was most marked with aortic involvement and less pronounced when only mitral lesions were present. Hypertrophy was more marked among male patients apparently because aortic lesions are more common among them. Proliferative inflammation of a nodular (Aschoff nodules) or diffuse type was common. The stigmas of rheumatic inflammation were practically as common in the valve and myocardium among calcified nodular aortic valve deformities as in mitral valve deformities. All nonsyphilitic aortic valvular deformities which lead to cardiac failure seem to be of rheumatic origin. Tricuspid and pulmonic lesions, especially healed deformities, rarely occur without associated aortic or mitral lesions.

American Journal of Pathology, Boston

16:525-708 (Sept.) 1940

Studies of Collagen: I. Production of Collagen in Vitro Under Variable Experimental Conditions. G. Hass and F. McDonald, Boston.—p. 525.

Id.: II. Methods and Results of Implantation of Collagen-Forming Cultures in Granulation Tissue. G. Hass, Boston.—p. 549.

Dermatomyositis: Study of Five Cases. T. D. Kinney and Mary M. Maher, New Haven, Conn.—p. 561.

Eosinophilic Granuloma of Bone: Report of Case. L. Lichtenstein and H. L. Jaffe, New York.—p. 595.

Comparative Experimental Studies of 200 Kilovolt and 1,000 Kilovolt Roentgen Rays: I. Biologic Effects on Epiphysis of Albino Rat. E. A. Gall, J. R. Lingley and J. A. Hilcken, Boston.—p. 605.

Familial Occurrence of Renal Carcinoma in Rhesus Monkeys (Macaca Mulatta). H. L. Ratcliffe, Philadelphia.—p. 619.

Teratoma of Ovary, with Segment of Vertebral Column and Remnants of Notochordal Tissue: Report of Case. J. L. Riopelle, Montreal. —p. 625.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

44:485-644 (Oct.) 1940

Roentgenology of Pancreatic Disease: Caldwell Lecture, 1939. J. T. Case, Chicago.—p. 485.
Recent Advances in Roentgen Examination of Neck: Body Section Roentgenography (Planigraphy) of Larynx. B. R. Young, Philadelphia.—p. 519.
Value of Proper Interpretation of Lipiodol Bronchograms in Thoracic Surgery, with Note on Distribution of Bronchiectasis. D. W. Myers and B. Blades, St. Louis.—p. 530.
Roentgenologic Study of Cystine Urinary Calculi. H. R. Morrison, Boston.—p. 537.
Vertebral Column in Acromegaly. W. Chester, Mamaroneck, N. Y., and E. M. Chester, New York.—p. 552.
Localization of Intra-Ocular Foreign Bodies with Contact Lens. R. L. Pfeiffer, New York.—p. 558.
Course of Besnier-Boeck's Disease of Lungs in Serial Roentgenograms. E. Meisels, Lwów, Poland.—p. 564.
Roentgen Ray in Obstetric Diagnosis. S. G. Schenck, Brooklyn.—p. 568.
Squamous Cell Epithelioma of Cervix Uteri with Bone Metastasis: Report of Two Cases. Elma Barany and A. M. Sala, New York.—p. 579.
Late Results in Supervoltage Roentgen Therapy: Comparative Statistical Analysis in Selected Groups. T. Leucutia, Detroit.—p. 586.
*Roentgen Therapy for Inflammatory Conditions: Further Considerations. A. U. Desjardins, Rochester, Minn.—p. 594.
Comparison of Skin Reactions Produced by 200 and 1,000 Kilovolt Radiations. R. S. Stone and J. M. Robinson, San Francisco.—p. 601.
Compact, Supervoltage, Roentgen Ray Generator Using a Pressure-Insulated Electrostatic High Voltage Source. J. G. Trump, R. J. Van de Graaff and R. W. Cloud, Cambridge, Mass.—p. 610.
Physical Characteristics of Supervoltage Roentgen Rays. J. G. Trump and R. W. Cloud, Cambridge, Mass.—p. 615.

Roentgen Therapy for Inflammatory Conditions.—According to Desjardins, when acute inflammatory processes, such as furuncles, carbuncles, abscess, erysipelas, parotitis, sinusitis, otitis media, pneumonia (especially delayed resolution in lobar pneumonia), are exposed early enough to a small dose of roentgen rays, rapid diminution of pain and resolution of the inflammation without suppuration follows in a large proportion. If the affected area is exposed after suppuration has developed, pain is relieved more slowly and suppuration is accelerated. When the inflammatory lesion is treated after suppuration has advanced, little or no change in the course of the process is perceived. The rate at which these alterations occur after irradiation corresponds closely to the rate at which lymphocytes, polymorphonuclear leukocytes and eosinophils are known to be affected after irradiation of normal animals. This agrees with the rate at which similar cells of human beings are influenced by irradiation. The influence, varying within certain limits with the dose of rays, consists in the destruction of a proportion of the leukocytes. Since the main effects of irradiation are exerted on cells, the sensitiveness of cells to irradiation is known to be specific for each type of cell and since the leukocytes are the only cells whose radiation sensitivity corresponds to that of acute inflammation it is concluded that the major effect of irradiating such lesions is the destruction of a proportion of the leukocytes infiltrating the inflamed tissues, of those circulating in the blood stream through and around these tissues and of the liberation of the contents of the destroyed leukocytes (antibodies, ferments and so on) into these tissues and into the blood stream. As for chronic inflammations amenable to irradiation, such as many cutaneous diseases, tuberculous adenitis, peritonitis, synovitis, keratitis and iritis, actinomycosis and many others, the pathologic circumstances differ in that leukocytic infiltration is less prominent, but the pronounced feature is proliferation of connective tissue. Connective tissue cells have such a low grade of sensitivity to radiation that they must be classed among the resistant cells. Therefore in chronic inflammatory lesions there is one factor, proliferation of connective tissue, which tends to diminish or retard the action of the rays. This is exactly what is observed in practice. The earlier chronic inflammations are treated, the better they respond. Too often, during the early stage of acute inflammations amenable to roentgen irradiation, the treatment is withheld until the inflammation has progressed beyond hope or until the best results of irradiation can no longer be expected. This situation will no doubt be corrected when more internists and surgeons become acquainted with and convinced of the value of roentgen therapy. A suitable dose of roentgen rays given in time may save some lives and in acute inflammatory processes a small or moderate dose given early will often make other treatment unnecessary.

Annals of Surgery, Philadelphia

112:801-976 (Nov.) 1940

Personal Experiences in Vascular Surgery: Statistical Synopsis. R. Matas, New Orleans.—p. 802.
*Clinical and Experimental Observations on Arteriovenous Fistulas. E. Holman, San Francisco.—p. 840.
*Surgical Treatment of Aneurysm of Abdominal Aorta: Review of Literature and Report of Two Cases, One Apparently Successful. I. A. Bigger, Richmond, Va.—p. 879.
Aneurysm of Abdominal Aorta: Treatment by Ligation. D. C. Elkin, Atlanta, Ga.—p. 895.
Aneurysm of Abdominal Aorta at Its Bifurcation into Common Iliac Arteries. R. Matas, New Orleans.—p. 909.
Experimental Studies on Gradual Occlusion of Large Arteries. H. E. Pearse, Rochester, N. Y.—p. 923.
Prevention of Ischemic Gangrene Following Surgical Operations on Major Peripheral Arteries by Chemical Section of Cervicodorsal and Lumbar Sympathetics. M. Gage and A. Ochsner, New Orleans.—p. 938.
Circulatory Disturbances Produced by Extensive Angiomas of Lower Extremities Associated with Varicose Veins. W. E. Lee and N. E. Freeman, Philadelphia.—p. 960.
Heparin in Prevention of Peritoneal Adhesions: Report of Progress. E. P. Lehman and F. Boys, Charlottesville, Va.—p. 969.
Duraluminum Enterotome for Devine Colostomy. M. Gage, New Orleans.—p. 975.

Arteriovenous Fistulas.—Holman states that since 1923, when Lewis and Drury presented observations on arteriovenous fistulas, 20 instances of this condition have been studied in man before and after their elimination, and numerous experimental animals have been observed before and after comparable fistulas were established between the larger vessels and permitted to remain for as long as seven years. Observations diametrically opposite to those of Lewis and Drury were made in some of the cases. Holman emphasizes the following points: 1. Complete cardiac decompensation with peripheral edema, ascites, hydrothorax and extreme cardiac dilatation may be corrected with a return of the heart to its normal size by eliminating a peripheral fistula. This dilatation involves not only the heart but the great vessels at its base. 2. Early evidence of the malignant influence of a fistula on the circulation—even before dilatation of the heart is detectable—is the behavior of the blood pressure and pulse following closure of the fistula by digital pressure. An increase in blood pressure and a fall in pulse rate indicate that the fistula is large and is one which is not likely to close spontaneously but is almost certain to produce increasing deleterious effects on the circulation. In 1 case, failure to heed this evidence in 1933 when the heart was normal and again in 1936 when the heart was beginning to dilate led to cardiac failure with marked dilatation in 1939. 3. This increase in blood pressure and fall in pulse rate constitute the first evidence that the circulatory bed is beginning to dilate, even though such dilatation may not yet be detectable by the usual means. 4. The extent of this increase and fall depends on the duration of the fistula and is commensurate with the extent of the dilatation of the heart and vessels proximal to the fistula being least in fistulas of short duration and greatest in those of long duration. 5. A temporary but great increase in blood pressure and fall in pulse rate may occur immediately following the operative elimination of a fistula, provided the operation is performed as a physiologic experiment without loss of blood. Despite operations for from four to six hours in 5 cases the blood pressure at the end of the operation was higher and the pulse slower than at the beginning, because of an autotransfusion from circulating blood which had increased in volume during the presence of the fistula. 6. This temporary increase and fall on closing a fistula are dependent on an increase in total blood volume, which is an inevitable accompaniment of a fistula of large size and long duration. 7. The increased blood volume is reduced immediately following operative removal of a fistula by a reduction in the plasma and a concentration of the erythrocytes and hemoglobin. 8. The increased blood volume may result in a transient overdistention of an already dilated heart following operative closure of a fistula, owing to a redistribution of the circulating blood, the volume of blood formerly diverted through the fistula into the capacious venous system now filling the central arterial bed. 9. Eight peripheral fistulas were eliminated by excision or ligature of segments of the main vessel to a limb

without any evident effect on the viability of the tissues beyond the ligature. In 1 case the common, deep and superficial femoral arteries were all ligated without nutritional impairment or function of the leg. This is explainable on the basis of the stimulus to collateral circulation that is provided by the area of diminished peripheral resistance at the site of the fistula, which attracts blood to it through all available channels. 10. When quadruple ligation of the vessels proximal and distal to the fistula is indicated, it would be desirable to ligate and divide the artery proximal to the fistula rather than to ligate it in continuity. In 1 case the fistula was reactivated by the ligature cutting through the arterial wall and reestablishing the lumen of the artery.

Surgery for Aneurysm of Abdominal Aorta.—According to Bigger, from 1817, when Sir Astley Cooper first ligated the abdominal aorta, to 1920 none of the 18 patients in whom the aorta was occluded for abdominal aneurysm survived to leave the hospital. Since 1920, 7 of 12 similar patients have been discharged from the hospital as improved and 1 other lived four and one half months but did not leave the hospital. While it is not certain that any of these patients have been cured, the results demonstrate that occlusion of the aorta is not necessarily fatal. The 2 of the 12 cases in which operation was performed by the author are reported. The first patient was a poor surgical risk in whom left-sided heart failure with pulmonary edema developed. He died following occlusion of the aorta proximal to the aneurysm. The other patient was a young man with a ruptured traumatic (gunshot) aneurysm. He had a preliminary occlusion of the aorta proximal to the aneurysm and one month later a restorative endo-aneurysmorrhaphy. One year later he appeared to be well, there was no evidence of aneurysm and the lumen of the aorta was obviously patent. The author realizes that traumatic and spontaneous aneurysms are widely different and that the treatment used for one may not be applicable for the other. For example, it is unlikely that a spontaneous aortic aneurysm would be suitable for reconstructive endo-aneurysmorrhaphy, but it seems likely that a few spontaneous aneurysms would be suitable for obliterative endo-aneurysmorrhaphy. Such procedures probably should not be attempted unless the aneurysm arises distal to the renal arteries and, almost certainly, not when the aorta is diffusely calcified. Proximal occlusion of the aorta should be a preliminary operation. This brings about shrinkage of the sac so that at the second operation the aorta or the common iliac arteries may be ligated immediately distal to the aneurysm. If the iliac arteries are permanently occluded the ligatures are to be placed on the common iliacs, and the internal iliacs (hypogastrics) should be carefully protected because of their importance as collateral channels. All possible vessels communicating with the sac should be ligated before the sac is opened. Aneurysms of the proximal portion of the abdominal aorta with such essential arteries as the celiac, superior mesenteric or both renals arising from the sac probably should not be treated surgically, while proximal ligation may be justified in aneurysms arising above the renal arteries but without any of the essential arteries originating from the sac. The author states that some of the problems of the surgical treatment of aneurysms of the abdominal aorta may be solved by carefully controlled animal experiments and others only by observations on patients with aortic aneurysms, especially those subjected to operation, and therefore careful reports of such cases are necessary. In his apparently recovered patient fascia was used to occlude the aorta at the first operation. The heavy silk ligature was left around the aorta to occlude it during the aneurysmorrhaphy in case the fascia no longer produced subtotal occlusion. The iliac arteries were exposed and heavy ligatures (tapes would have been better) passed around them for the control of retrograde bleeding when the sac was opened. In spite of these precautions there was considerable pressure in the aorta, presumably from the lumbar and middle sacral arteries which entered the aorta below the occlusion. The author is of the opinion that the strip of fascia has now completely disappeared and that the lumen of the aorta is fully restored.

Archives of Dermatology and Syphilology, Chicago

42:755-992 (Nov.) 1940

Lichen Sclerosus et Atrophicus. H. Montgomery and W. R. Hill, Rochester, Minn.—p. 755.
Personality Factor in Psychoneurogenous Reactions of Skin. J. H. Stokes, Philadelphia.—p. 780.
*Parenteral Use of Hypertonic Dextrose for Relief of Pruritus and Serum Sickness. O. M. Stout and R. J. Kositchek, Los Angeles.—p. 802.
Sensitization to Arsenical Compounds: Sensitization to Pentavalent Arsenical Following Use of Trivalent Arsenical. A. G. Franks and S. Fisher, New York.—p. 808.
"Bubonulus" in Lymphogranuloma Venereum. R. Brandt, Augusta, Ga.—p. 811.
Arsphenamine Encephalopathy: Report of Unusual Clinical and Histologic Observations. N. A. Levy, Chicago.—p. 814.
Epithelioma Adenoides Cysticum, Tricho-Epithelioma and Basal Cell Cancer: Relation Between These Diseases as Shown by Histologic Studies of Multiple Benign Cystic Epithelioma. H. L. Traenkle, Buffalo.—p. 822.
Staphylococcic Impetigo Contagiosa. S. Epstein, Marshfield, Wis.—p. 840.
Pseudo-Epitheliomatous Hyperplasia. L. H. Winer, Minneapolis.—p. 856.
Mobilization of Bismuth Produced by Ammonium Chloride. E. F. Corson, Philadelphia; H. B. Decker, Camden, N. J., and T. L. Williams, Philadelphia.—p. 868.
Transverse Furrows of Nails. Z. T. Wirtschafter and S. Littman, Cleveland.—p. 874.
Human Infection with Ecthyma Contagiosum, a Virus Disorder of Sheep: Report of Two Cases. R. Nomland, Iowa City.—p. 878.
Epidermolysis Bullosa: Clinical and Bacteriologic Study: Report of Four Cases. A. B. Cannon, M. Sanders and J. L. Rankin Jr., New York.—p. 884.
Experimental and Clinical Observations with Histaminase. A. F. Knoll and L. G. Beinhauer, Pittsburgh.—p. 896.
Effects of Neoarsphenamine and Mapharsen on Formed Elements of Blood: Granulocytopenia Following Neoarsphenamine Therapy in Patient Who Subsequently Received Mapharsen Without Untoward Reaction. N. N. Epstein and E. H. Falconer, San Francisco.—p. 909.
Mapharsen in Treatment of Forty Patients Following Arsphenamine Dermatitis. A. G. Schoch, L. J. Alexander and W. E. Long, Dallas, Texas.—p. 919.
*Herpes Progenitalis as a Venereal Contagion. H. Sharlit, New York.—p. 933.

Hypertonic Dextrose for Pruritus and Serum Sickness.—Stout and Kositchek observed the therapeutic effect of hypertonic solution of dextrose on patients with serum sickness and certain types of pruritus. A 5 per cent solution of dextrose by hypodermoclysis relieved the itching of a patient with exfoliative dermatitis of unknown cause. Thereafter the effects of the solution on patients with other pruritic diseases were determined. The results have been sufficiently consistent and have been sufficiently controlled to represent reliable material. In some of the cases the response of objective signs (urticaria) have paralleled the response of the subjective manifestations. The authors have not been able to establish the theoretical basis for the results. At first a 5 per cent solution of dextrose was used subcutaneously; later it was found that the intravenous route was more efficacious. The usual procedure was to administer 50 cc. of a 50 per cent solution of dextrose and to repeat this, when indicated, or to administer larger quantities of 5 or 10 per cent solutions. In several instances the effects were so instantaneous as to suggest a psychic factor. This factor was ruled out in that isotonic saline solution had no effect in 15 control cases. Of 58 patients who presented pruritus as a prominent symptom 43 were satisfactorily relieved and 15 experienced no relief. Of the 43 who responded satisfactorily, 10 had serum sickness, 7 pityriasis rosea with severe pruritus, 4 pruritus ani, 3 pruritus vulvae, 3 generalized urticaria, 3 dermatitis medicamentosa, 3 generalized exfoliative dermatitis, 2 generalized seborrheic dermatitis and 1 each generalized lichen planus, pruritic papular secondary syphilis, keratoderma climactericum, neoplastic obstructive jaundice, lymphoblastoma cutis, vegetative pemphigus, dermatitis herpetiformis and generalized erythema multiforme. Of the 15 who failed to respond, 5 had infectious eczematoid dermatitis, 4 poison oak dermatitis, 5 senile pruritus, 1 pruritus vulvae, 1 generalized seborrheic dermatitis and 1 atopic eczema with asthma. In the controls after 50 cc. of isotonic saline solution was given intravenously neither objective nor subjective relief was obtained. From one half to several hours after the saline solution was given dextrose was administered with immediate results. In 4 cases in which itching had been a prolonged symptom and in which periodic injections of dextrose controlled the pruritus, substitution of saline solution without the patient's knowledge demonstrated that the dex-

trose produced relief and the saline solution did not. The most noteworthy results were obtained by the 10 patients with serum sickness. The results were immediate, consistent and complete; not only was the pruritus relieved but the accompanying pains in the joints, urticaria and fever. Three of them had previously failed to respond to intensive treatment with epinephrine and calcium gluconate.

Herpes Progenitalis as a Venereal Contagion.—Sharlit believes that the evidence he presents unequivocably establishes herpes progenitalis as a venereal contagion. He presents the histories of 2 patients whose reliability of the pertinent facts argues acceptance of the venereal source of herpes progenitalis and suggests that this clinical entity be included in the group of venereal diseases. The histories are as follows: In February 1928 a white man immediately after sexual intercourse noticed a papule on his penis. That night lightning pains developed in the right groin, and the next morning, when he called on the author, he observed a slight swelling in the right inguinal region. Examination showed a solitary papule on the dorsal surface of the shaft of the penis which was capped by a ruptured vesicle. The skin about the base of the papule was deeply red; a burning pain was present in the lesion and pains radiated to the right groin. The right inguinal nodes were enlarged and tender. The patient had never had a genital "sore" of any kind before. In the preceding twelve months the patient, with one exception, had had sexual relations with only one woman. The exception occurred just six days before his appearance at the author's office. A dark field examination of the lesion showed no spirochetes. A Wassermann test of the woman "of a week ago" was negative. She refused to be examined. A provisional diagnosis of genital herpes was made. Five days after the patient's first visit he returned and brought with him the woman of his constant attention. The night before she had a burning pain in the right vulvar region and on examination an eruption was revealed; tiny vesicles on a deeply congested background on the right labium majus. The condition was typical herpes simplex, the first and only herpes progenitalis that the author has seen in a woman. This woman had never had a genital lesion. The woman's history extended for but one year from her first visit, during which time she had one recurrence of genital herpes in approximately the same region. The man's history has now been available for twelve years. During this time he has had at least a dozen recurrences of herpes progenitalis, on the shaft and on the corona. He has never again had a solitary papule covered by a vesicle but always grouped vesicles. The last two attacks, however, have been on the right buttock. The author believes that his cases are evidences of contagious inoculation, albeit apparently the first. He sees in them missing links in the chain of a rationalized epidemiology. He hopes that careful and detailed studies of the histories of cases of herpes progenitalis will be made to the end that the epidemiology of their infectiousness may be convincingly clarified. The pertinent facts of 2 cases from the private records of Charles Rein of New York are given: A woman, receiving treatment for frequently recurring genital herpes, married during the period of treatment. Nine months after marriage an initial attack of penile herpes occurred in the husband and was followed by recurrences. The rarity of genital herpes minimizes coincidence as explanatory of these 2 cases in connubium. The fact that the husband had approximately nine months of exposure before becoming infected has immunologic significance.

Archives of Pathology, Chicago

30:993-1158 (Nov.) 1940

Giant Cell Tumor of Bone: Its Pathologic Appearance, Grading, Supposed Variants and Treatment. H. L. Jaffe, L. Lichtenstein and R. B. Portis, New York.—p. 993.
Factors Governing Solubility of Human Gallstones in Dog's Bile. H. G. Aronson, Chicago.—p. 1032.
Wave Mechanics in Striated Muscle: XVI. Effects of Experimental Variations in Temperature and of Microcapillarity on Cross Striations in Muscle. E. J. Carey, Milwaukee.—p. 1041.
Pigmented Cells of Pia and of Meningeal Tumors. A. E. Taft, Philadelphia.—p. 1073.
Role of Fixed Tissue Phagocytes in Lipid Metabolism. E. F. Hirsch and S. Weinhouse, Chicago.—p. 1079.
Lysozyme and Its Relation to Antibacterial Properties of Various Tissues and Secretions. R. Thompson, New York.—p. 1096.

Archives of Surgery, Chicago

41:1043-1304 (Nov.) 1940

Diseases of Esophagus: Esophagoscopic Considerations. L. H. Clerf, Philadelphia.—p. 1043.
*Congenital Atresia of Esophagus: Study of Thirty-Two Cases. T. H. Lanman, Boston.—p. 1060.
Roentgen Demonstration of Esophageal Varices: Its Clinical Importance. R. Schatzki, Boston.—p. 1084.
*Bleeding Esophageal Varices: Evaluation of Methods Directed Toward Their Control, Especially by Direct Injection of Sclerosing Solution. W. Walters, H. J. Moersch and D. A. McKinnon, Rochester, Minn.—p. 1101.
Esophageal Diverticula. F. H. Lahey, Boston.—p. 1118.
Conservative Treatment of Achalasia. E. B. Freeman, Baltimore.—p. 1141.
Surgical Considerations of Achalasia: Review of Literature and Report of Three Cases. A. Ochsner and M. DeBakey, New Orleans.—p. 1146.
Surgical Treatment of Carcinoma of Esophagus. J. H. Garlock, New York.—p. 1184.
Malignant Tumors of Hernial Sacs. L. M. Zimmerman and H. Laufman, Chicago.—p. 1215.
Congenital Absence of Sacrum. I. M. Zeligs, Iowa City.—p. 1220.
Femoral Hernias: Study of 238 Hernias and 226 Repairs. H. J. Shelley, Fort Worth, Texas.—p. 1229.
Parenteral Administration of Water-Soluble Compound with Vitamin K Activity: 4-Amino-2-Methyl-1-Naphthol Hydrochloride. E. R. Anderson, J. E. Karabin, H. Udesky and L. Seed, Chicago.—p. 1244.
Role of Intraluminal Obstruction in Pathogenesis of Acute Appendicitis. H. Koster and A. Shapiro, Brooklyn.—p. 1251.
Fibrosarcoma of Soft Tissue Producing Regional Concentric Bone Absorption. O. C. Julian, Chicago.—p. 1257.
Review of Urologic Surgery. A. J. Scholl, Los Angeles; F. Hinman, San Francisco; A. von Lichtenberg, Budapest, Hungary; A. B. Hepler, Seattle; E. Gutierrez, New York; G. J. Thompson, J. T. Priestley, Rochester, Minn.; E. Wildbolz, Bern, Switzerland, and V. J. O'Conor, Chicago.—p. 1272.

Congenital Atresia of Esophagus.—Lanman presents an analysis of 32 cases of congenital atresia of the esophagus observed at the Children's Hospital during the last eleven years. Thirty of the patients were submitted to operation. A complete necropsy was performed on 2. The observations on the 30 operative cases were supplemented by complete postmortem examination of 22. Despite the fatal outcome in all of the 30 operative cases, the author believes that considerable progress along rational lines is being made and that successful operative treatment is only a question of time. For a successful outcome it is essential that the condition be recognized during the first few hours of life. Any infant presenting characteristic signs or symptoms of esophageal atresia should have a catheter passed down the esophagus and roentgenograms performed without opaque medium. Immediate operation is imperative if obstruction is present. The author states that anterior gastrostomy is futile unless the lower segment does not communicate with the trachea. Regardless of what procedure other than a direct anastomosis is used for the lower segment, the upper segment must be treated so that aspiration of the overflow of secretions from this blind pouch is prevented. Constant suction is dangerous. Early exteriorization of this upper segment has been advocated and used at the Children's Hospital without success, though, the author states, it is possible that it would have been successful in three of the cases had a posterior esophagostomy not been added to the closure of the fistula at the first operation. Exteriorization of the upper segment commits the patient, if he survives, to a permanent exterior esophagus. Treatment of the lower segment, except in cases with a blind end to the upper and lower segments of the esophagus and in those in which the upper segment communicates with the trachea and the lower segment is blind, must include measures which will prevent contents from the lower segment from entering the trachea. Some of the procedures suggested do not do this. It is the author's belief that no method of attack that does not have as its first step direct closure of the fistula between the lower segment and the trachea has any reasonable chance of success, particularly as regards a primary anastomosis. Direct exposure of the fistula by the extrapleural approach, he believes, should be undertaken. The extrapleural approach seems to be safer than the transpleural. If direct anastomosis is possible it should be done, and if successful and no complication develops the problem is solved, barring possible esophageal stenosis later. If direct anastomosis appears impossible or inadvisable the tracheoesophageal fistula should be closed and nothing further done at this time. Subsequent procedures as soon as conditions permit are exteriorization of the upper esophageal segment and

anterior gastrostomy. If the patient survives, construction of an exterior connection between the upper esophagostomy and the anterior gastrostomy can then be postponed until a suitable age. An exterior esophagus as a palliative procedure for an elderly patient with cancer is justifiable and endurable, but one dreads to commit an infant to such an existence.

Bleeding Esophageal Varices.—Walters and his associates conclude that esophageal varices develop as a result of obstruction of the portal and splenic veins and that bleeding occurs because of their superficial position in relation to the esophageal mucosa. Banti's disease and splenic anemia are frequently associated with esophageal varices. They cannot be regarded as distinct clinical entities, as they may result from obstruction of the portal or splenic vein. The surgical treatment of splenic anemia has been directed toward removal of the enlarged spleen. Although it has been followed by good results in a large series of cases, the operation does not prevent recurrence of bleeding from the esophageal varices in more than 38 per cent of the cases even when combined with ligation of the coronary vein or with omentopexy. According to Mayo, in about 10 per cent of the cases in which recovery has taken place after splenectomy, death has occurred some time in the next ten years of hemorrhage from the stomach, probably from ruptured varices in the lower end of the esophagus. Although ligation of the coronary vein in the gastrohepatic omentum will serve to interrupt considerable flow of blood through it, the procedure has been used alone in too few cases of splenic anemia to justify any conclusion of its merits in reducing the incidence of hemorrhages from esophageal varices. The recent successful obliteration of esophageal varices by injecting sclerosing solutions into them through the esophagoscope, and their use of the method in 6 cases, lead the authors to believe that the procedure is worthy of trial. Sufficient time has not elapsed to determine whether further bleeding will occur making repetition of the method necessary. The authors believe that the procedure offers a method of controlling bleeding that has not responded to any other form of therapy and thus may be successful in prolonging the life of the patient.

Arkansas Medical Society Journal, Fort Smith

37:113-134 (Nov.) 1940

Medical Education in the United States 1934-1939. S. P. Cromer, Little Rock.—p. 113.
Diagnosis and Treatment of Ectopic Pregnancy. B. L. Moore, El Dorado.—p. 116.

Bulletin New York Academy of Medicine, New York

16:657-720 (Nov.) 1940

Pathologic Aspects of Rheumatic Fever. C. E. de la Chapelle, New York.—p. 659.
Treatment of Mental Disease in France at the End of the Eighteenth Century. C. P. Oberndorf, New York.—p. 670.
Review of Maternity Statistics of New York City for the Year 1939. T. J. Duffield, New York.—p. 679.

Connecticut State Medical Journal, Hartford

4:637-706 (Nov.) 1940

Beginnings of Medical Practice in New Haven Colony. H. Thoms, New Haven.—p. 639.
Emergency Treatment of Fractures. C. R. Murray, New York.—p. 645.
*Results of Four Types of Therapy in 165 Cases of Pneumonia. P. J. Steincrohn, Hartford.—p. 653.
Fundamental Principles of Treatment of Gonococcic Infections of Women. R. M. Lewis, New Haven.—p. 662.
Problems Relating to Diphtheria Toxoid Immunization. M. M. Hillman, New Haven.—p. 664.
Treatment of Compound Fractures. D. C. Patterson, Bridgeport.—p. 666.
Tumors of Lateral Aberrant Thyroid Tissue: Report of Two Cases. W. A. Geer, Bridgeport.—p. 670.

Four Types of Therapy for Pneumonia.—Steincrohn discusses four types of treatment used for 165 pneumonia patients treated in his medical service at the Municipal Hospital during February, March and April of the years 1934 to 1939. The treatments were routine, concentrated dextrose intravenously, serum and sulfapyridine. The mortality for 1934 through 1938 was 35 per cent for all ages. Among patients less than 60 years of age the rate was 20.4 per cent, rising to 60.3 per cent in those more than 60. The mortality in patients with coexisting disease was 42.1 per cent as against 17.6 per cent free from complications. Although the mortality rate for the dextrose treated patients was higher (38.4 per cent) than those routinely treated (32.4 per cent) intravenous dextrose therapy has its place in the treatment of individual indications. The average age of the 46 patients who died during the 1934 to 1938 period was 49.3 years and of the 29 given sulfapyridine in 1939 it was 52.3 years. In view of the fact that almost 50 per cent of the patients in the latter group were more than 60 years of age, the sulfapyridine mortality of 8.3 per cent (excluding death within twenty-four hours of admission) is startling as compared with the revised mortality of 30.2 per cent for the patients receiving routine dextrose and serum treatment. In his small series the author observed a definite leukocytic response to sulfapyridine. In the majority of patients who recovered there was a relative leukopenia in from twenty-four to forty-eight hours. The author felt that the absence of a leukopenic response made for a poor prognosis. A marked leukopenia with a normal differential count is no contraindication to the further administration of sulfapyridine. A high concentration of sulfapyridine in the blood does not necessarily indicate a good prognosis. The average number of days of illness before admission in the entire series was practically the same. Patients treated with sulfapyridine were free from fever in an average of 1.6 days, and the 1934 to 1938 group in 9.4 days. The mortality rate of 17.6 per cent among the serum treated patients bears out the accepted experience that serum treatment cuts routine treatment mortality in half. The comparative results of the four treatments demonstrates that no patient with pneumonia should be deprived of the unquestionable aid of sulfapyridine or serum therapy.

Delaware State Medical Journal, Wilmington

12:213-230 (Oct.) 1940

Complicated Labor, with Special Reference to Use of Forceps. C. H. Davis, Wilmington.—p. 213.

Endocrinology, Los Angeles

27:707-842 (Nov.) 1940. **Partial Index**

Study of Metabolism of Crystalline Progesterone. Eleanor H. Venning and J. S. L. Browne, Montreal.—p. 707.
Effect of Estrogens on Pregnandiol Output During the Menstrual Cycle. C. J. Pattee, Eleanor H. Venning and J. S. L. Browne, Montreal.—p. 721.
Alteration of Urinary Excretion of Androgens by Estrogenic Therapy. E. C. Hamblen, Durham, N. C.; C. J. Pattee, Montreal, and W. K. Cuyler.—p. 734.
*Oral Administration of Diethylstilbestrol Dipropionate. B. B. Weinstein, J. C. Weed, F. R. Lock and C. G. Collins, New Orleans.—p. 739.
Castration in the Male: Notes on Hypothalamicopituitary-Gonadal System. R. C. Moehlig, Detroit.—p. 743.
Endocrine Dyscrasia of Acne Vulgaris in Women. C. H. Lawrence and N. T. Werthessen, Boston.—p. 755.
Blood Sugar Studies in Case of Adiposogenital Dystrophy Showing Chronic Hypoglycemia. J. F. Hart, New York.—p. 759.
*Treatment of Obesity Due to Dietary Indiscretion (Overeating) with Benzedrine Sulfate. J. S. Ersner, Philadelphia.—p. 776.
Does Testosterone Propionate Inhibit Ovulation? H. O. Burdick, Alfred, N. Y.—p. 825.

Oral Administration of Diethylstilbestrol Dipropionate.—Weinstein and his associates gave diethylstilbestrol dipropionate orally to 51 women complaining of physiologic menopausal symptoms, to 35 having menopausal symptoms that were initiated by roentgen or surgical treatment, to 6 young women suffering from hypo-estrogen symptoms and to 8 women with atrophic genital changes. The therapeutic regimen for the first group consisted of 1 mg. of diethylstilbestrol dipropionate three times a day. After one week the patient's response to the medication was ascertained and further dosage varied with the individual's reaction. When symptoms were mild or markedly improved the daily dose was reduced to 0.3 mg., whereas the daily dose of those giving little or no response was increased to as much as 15 mg. Twenty-five of these patients were relieved of all symptoms, 16 were improved, 3 showed only slight improvement and 7 exhibited no response. The basis of the treatment of patients with artificial menopausal symptoms was that employed for the preceding group. Individualization of therapy was followed. Generally a large maintenance dose was necessary for relief of this group; 19 were completely relieved, 13 were improved, 2 were slightly improved and 1 experienced no improvement. For the 6 young women exhibit-

ing evidence of hypo-estrogenism (as manifested by menstrual irregularities, headaches, nervousness, irritability, occasional hot flushes, anxiety, depression and diminished libido) individualization of therapy was essential. As most of the complaints were of a cyclic nature, usually preceding or associated with the menstrual flow, the drug was used at that time. All 6 were improved. The atrophic changes of the genitalia in 3 of the 8 women followed artificial menopause, 4 were associated with the physiologic menopausal syndrome and 1 exhibited senile vaginitis without concomitant menopausal symptoms. Here again therapy was individualized. Keratinization of the vaginal epithelium followed the oral administration of the drug. This was observed within as short an interval as one week, and with as little as 7 mg. of the drug. Usually three weeks elapsed and 21 mg. of the drug was necessary before complete relief was obtained. All patients were completely relieved, but recurrences were frequent in from six to twelve weeks after treatment was stopped. Diethylstilbestrol dipropionate orally controls the senile vaginitis, and keratinization of the vaginal epithelium takes place, but the associated atrophic changes do not show the same degree of regression that follows the vaginal administration of biologic estrogens. The only toxic manifestations evidenced by 15 per cent of the women were nausea and vomiting. Only 1 patient was completely intolerant to the drug.

Amphetamine Sulfate for Obesity.—Ersner states that in more than 500 cases of obesity amphetamine sulfate has proved to be the "drug of choice" in obtaining excellent results. No serious complications were encountered. Only obese patients who gave a history of overeating were selected for treatment. After a physical examination the patient was put on a diet of from 1,200 and 1,500 calories daily. This diet consisted of dry cereals, skimmed milk, tea or coffee (without sugar or cream) fresh and stewed fruits, raw and cooked vegetables, one slice of bread with each meal and the choice of from 6 to 8 ounces of meat, fish, chicken, cottage cheese or two eggs daily. The patient was cautioned to limit the intake of fluid and to make certain of a daily evacuation. The patient was given the first week's medication (the smallest possible dose) and thereafter returned every week for a check-up and further medication. The drug was withdrawn at the end of every month or the loss of the first 20 pounds (9 Kg.) and subsequent 15 pounds (6.7 Kg.), and for the ensuing week some brand of vitamin B, C and G was prescribed to make up for any deficiency in the diet caused by the patient's carelessness. After each of these vitamin periods the previous week's dosage was again prescribed and then increased the following week. This permitted the final strength of the drug, one 10 mg. tablet after each meal, to be reached in about three months. The amount of weight to be lost at any one course of treatment was never to be more than one fifth or one sixth of the patient's greatest weight. If the new final weight was far from the nearest calculated normal chart weight (according to height and age), the patient was instructed to return in from four to six months, when again this procedure would be repeated. Thus no patient in the series showed any untoward effects from the loss of weight, even though as much as 60 pounds (27 Kg.) was lost by 1 patient in the course of three months. The average weight lost for the first week amounted to 5 pounds (2.3 Kg.). The average loss for a course of treatment (from three to twelve weeks) was 3½ pounds (1.4 Kg.) per week. With the exception of the vitamin week there were but few occasions when a continuous and sustained loss of weight was not obtained; 100 per cent cooperation was requested. Invariably most of the patients would voluntarily say that they were feeling much better or had much more pep. All agreed that the loss of appetite made dieting easy. With the small graduated doses of amphetamine sulfate employed, the systolic and the diastolic readings, when hypertension was present, usually dropped to normal. Whether this drop toward normal was directly due to the action of the drug or to the loss of weight is a question. Several instances of hypotension became normal during the course of treatment. Normal blood pressures were not affected or were slightly, if at all, lowered. There was but little change in the metabolic rate during the course of treatment. A marked progressive improvement in urines containing albumin, sugar and hyaline and granular casts was observed, indicating that amphetamine sulfate produces no injurious renal effects. There was little evidence of true addiction. In most instances the medication caused a mild constipation, which was easily remedied with a mild laxative or a simple lubricant, as liquid petrolatum. The reported untoward reactions of the drug should be of much significance to the dispenser and the novice who is about to prescribe it. The patient must be educated as to the possibility of its allergic reactions and of its cumulative effects. Self medication and overdosing must be eliminated to prevent any future fatalities.

Indiana State Medical Assn. Journal, Indianapolis

33:603-644 (Nov.) 1940

World Affairs and Medicine. K. R. Ruddell, Indianapolis.—p. 603.
Acute Nephritis. J. M. Hayman Jr., Cleveland.—p. 605.
Evolution and Revolution in Medical Practice. N. K. Forster, Hammond.—p. 609.
Roentgenologic Aspects of Pulmonary Mycotic Infection. R. C. Beeler, J. N. Collins and W. M. Loebr, Indianapolis.—p. 613.
Auriculoventricular Heart Block with Stokes-Adams Syndrome in Patient with Syphilitic Heart Disease and Diffuse Myocarditis. C. Bohnengel, New York.—p. 617.
*Relationship Between Various Types of Kidney Disease and Hypertension. W. L. Ritter, Indianapolis.—p. 620.
Anent Pronunciation of Medical Words. M. Thebaut, Oakland, Calif.—p. 623.

Kidney Disease and Hypertension.—Ritter studied the relationship between urologic abnormalities and arterial hypertension. He analyzed data from 28 patients with such abnormalities and from 24 patients suffering from hydronephrosis or renal anomalies with or without stones or secondary infection. The patients in the first group had developmental urinary anomalies. Among them there were 4 who had elevated blood pressures, more than 140 systolic and more than 90 diastolic. These cases give an incidence of 14.2 per cent, which is not greater than that which occurs among the apparently normal population. Persons with renal anomalies are apparently not appreciably more subject to hypertension than are normal people. The patients of the second group were admitted to the Indianapolis City Hospital from five to ten years ago and were chosen because at the time of their first observation their blood pressures were normal, less than 140 systolic and 90 diastolic. Blood pressure elevations did not develop in any of these patients during the interval, although many had had recurrent urinary infections or lithiasis and colic. The author concludes that since neither renal anomalies nor hydronephrosis with or without lithiasis or infection leads to hypertension an increased incidence of pyelographic abnormalities among patients with hypertension might be better explained by the assumption that the humoral substances responsible for hypertension may also act on the kidneys and ureters to produce these distorted shadows.

Johns Hopkins Hospital Bulletin, Baltimore

67:309-376 (Nov.) 1940

Sickling Phenomenon, with Special Reference to Differentiation of Sickle Cell Anemia from Sickle Cell Trait. I. J. Sherman, Baltimore.—p. 309.
Immunity in Relation to 1:2:5:6-Dibenzanthracene-Induced Sarcomas. Margaret Reed Lewis, Baltimore.—p. 325.
*Electrolyte Changes in Pulmonary Tuberculosis, with Special Reference to Adrenal Cortical Function. G. W. Thorn, R. P. Howard, Baltimore, and H. Dayman, Ray Brook, N. Y.—p. 345.
Chemotherapy of Experimental Escherichia Coli Infections in Mice. H. F. Klinefelter, Baltimore.—p. 365.
Distribution of Pigmentation on Arm and Thorax of Man. P. H. Futcher, Baltimore.—p. 372.

Electrolyte Changes in Pulmonary Tuberculosis.—Thorn and his associates investigated the blood serum concentration of sodium, chloride, potassium, carbon dioxide combining power and plasma volume of 104 patients with pulmonary tuberculosis in an effort to determine whether adrenal cortex insufficiency existed. Nine healthy men living in the same environment and 7 patients suffering from widespread nontuberculous pulmonary disease (silicosis) were chosen as controls. Because the menstrual cycle has a marked effect on electrolyte balance, only male patients were used for the study. All the patients were provided with an adequate intake of sodium chloride during a preliminary control period. A summary of the observations revealed a significant decrease in serum chloride concentration in patients with pulmonary tuberculosis and in patients with extensive nontuberculous pulmonary disease. The

decrease in serum chloride paralleled closely the decrease in the vital capacity of these patients. The serum bicarbonate concentration of patients with extensive pulmonary disease was increased but it did not equal in magnitude the reduction in serum chloride. There was no significant alteration in the concentration of serum sodium or potassium in either group. The hematocrit (percentage cell volume) of patients with pulmonary tuberculosis and extensive nonpulmonary disease was greater than normal. Blood volume studies and examination of the erythrocytes usually indicated an increase in their number and in their total volume. This was associated with a corresponding decrease in the volume of blood plasma. In 48 of 60 patients with pulmonary tuberculosis, a three day regimen of low sodium chloride intake with supplementary potassium did not precipitate signs or symptoms of adrenal cortex insufficiency. With the exception of a considerable decrease in serum chloride concentration the changes in serum electrolytes, body weight and blood pressure during this period were within normal limits. The urinary concentrations of sodium and chloride on the third day of the test were also within normal range. The appreciable weight loss, the higher than normal urinary concentration of sodium and chloride and the anorexia and weakness which occurred in 2 patients suggested that they may have had some degree of adrenal cortex insufficiency. Patients with pulmonary tuberculosis differed from those with Addison's disease in that they maintained a normal serum concentration of sodium and potassium, preserved a normal total blood volume and withstood a regimen of sodium chloride deprivation with supplementary potassium medication without changes in body weight, blood pressure and urinary concentration of sodium and chloride typically observed in adrenal cortex insufficiency. When acidosis or renal disease is absent the response to the Cutler, Power and Wilder sodium chloride deprivation test is of great aid in differentiating patients with pulmonary tuberculosis from those in whom the pulmonary tuberculosis is complicated by adrenal cortex or anterior pituitary deficiency.

Journal of Clinical Investigation, New York

19:795-888 (Nov.) 1940

*Origin and Nature of Normal Human Synovial Fluid. Marian W. Ropes, Elsie C. Rossmeisl and W. Bauer, Boston.—p. 795.
Excretion of Sodium Pregnandiol Glucuronidate in Urine of Normal Human Pregnancy. C. Bachman, Dorothy Leekley and H. Hirschmann, Philadelphia.—p. 801.
*Effect of Large Doses of Vitamins A, B, C and D on Incidence of Upper Respiratory Infections in Group of Rheumatic Children. Ann G. Kuttner, Irvington-on-Hudson, N. Y.—p. 809.
Carbohydrate Metabolism in Addison's Disease. G. W. Thorn, G. F. Koepf, R. A. Lewis and Elizabeth F. Olsen, Baltimore.—p. 813.
Choline Esterase of Blood Cells and Plasma in Blood Dyscrasias, with Special Reference to Pernicious Anemia. Jean Captain Sabine, Rochester, N. Y.—p. 833.
Fat Metabolism in Diabetes Mellitus. W. C. Stadie, Philadelphia.—p. 843.
Basal Gastric Secretion as Clinical Test of Gastric Function, with Special Reference to Peptic Ulcer. A. L. Bloomfield, Chen Kuo Chen and L. R. French, San Francisco.—p. 863.

Origin and Nature of Normal Human Synovial Fluid.—In an endeavor to determine whether the synovial fluid of human beings is a dialysate of plasma containing albumin, globulin and mucin, as is bovine synovial fluid, Ropes and her associates studied the synovial fluid immediately after death of 124 patients who had had no signs or symptoms of joint disease. The study indicated that bovine and human synovial fluids are essentially the same, as the distribution of nonelectrolytes and electrolytes between plasma and normal human synovial fluid were in accord with the observations in normal bovine synovial fluid. Normal human synovial fluid is a dialysate of blood plasma and contains albumin, globulin and mucin. The presence of mucin distinguishes synovial fluid and similar connective tissue fluids from other body fluids that are dialysates of plasma.

Vitamins and Respiratory Infections.—Kuttner studied the effect of adding an excess of vitamins A, C, D and B complex to an average diet of half of 108 rheumatic children from 7 to 14 years of age admitted for institutional care, who remained in the institution from December until the end of May. Children with definite histories of one or two attacks of polyarthritis or carditis without severe cardiac damage were selected. The effect of the addition of the vitamins was studied during two successive winters. Half of the 108 children received the regular diet with the addition of vitamins, and the other half received the regular diet but were given no additional vitamins. The children in the two groups were matched as nearly as possible as to rheumatic history, age and general condition. Beginning in February 1939 and continuing through May, infections of the upper respiratory track developed in 32 children. These infections were associated with the presence of group A beta hemolytic streptococcus of a single type, type 4. Most of the children complained of sore throat and had temperatures of from 101 to 103 F. for two or three days accompanied by elevated leukocyte counts. Type 4 streptococci were isolated from throat cultures and were usually present in large numbers. Rheumatic manifestations following these respiratory infections did not develop in any of the 32 children. The average gain in weight during the five months for the boys in the two groups was the same. The average weight gain among the girls receiving vitamins was 1½ pounds (0.7 Kg.) more than among those serving as controls. During the winter of 1939-1940 two types of respiratory infections were prevalent among the children: an outbreak of 51 cases of influenza (characterized by fever, malaise and a low leukocyte count) and 24 sore throats accompanied by fever and elevated leukocyte counts. Throat cultures from the influenza cases were negative for beta hemolytic streptococci. Throat cultures from the cases of pharyngitis showed group A beta hemolytic streptococci of a single type, type 27. Of the 13 children who were not receiving vitamins and who contracted type 27 infections a rheumatic recurrence following a latent period developed in only 1. Of the 11 children who were receiving vitamins and who contracted type 27 infections, rheumatic recurrences following a latent period developed in 3. The latent periods were respectively, eighteen, twenty-two and twenty days. The administration of vitamins to these 3 children was never interrupted and therefore the rheumatic recurrence developed in spite of the administration of large amounts of vitamin C. Of the 51 children who had influenza, 26 were receiving vitamins and 25 were in the control group. In contrast to the previous year, the average gain in weight of the boys receiving vitamins was slightly greater than of the control boys and the gain in weight among the two groups of girls was the same. Children receiving institutional care usually tend to gain and therefore no definite improvement can be attributed to the vitamins. No evidence was obtained suggesting that the addition of large doses of vitamins A, B complex, C and D to an ordinary well balanced diet reduces the incidence of infections of the upper respiratory tract.

Journal Industrial Hygiene & Toxicology, Baltimore

22:303-380 (Oct.) 1940

Control of Tuberculosis: I. Pulmonary Tuberculosis in Applicants for Employment. Ada Chree Reid, New York.—p. 303.
Physiologic Response of Animals to Some Simple Mononitroparaffins and to Certain Derivatives of These Compounds. W. Machle, E. W. Scott and J. Treon, Cincinnati.—p. 315.
How Toxic Is Arsenate of Lead? I. D. Cardiff, Yakima, Wash.—p. 333.
Chemical and Physiologic Investigation of Electric Arc Welding: I. Bare, Washed Welding Rods. G. C. Harrold, S. F. Meek and C. P. McCord, Detroit.—p. 347.

Journal of Infectious Diseases, Chicago

67:81-176 (Sept.-Oct.) 1940

Abrupt Increase in Resistance to Crotalus Venom. P. Kyes, L. Markin and O. J. Graham, Chicago.—p. 81.
Survival of Pneumococci in Empyemic Fluid: Effect of Sulfapyridine on Their Viability. E. Neter, Buffalo.—p. 84.
Failure of Shocking Agents to Influence Mode of Spread of Various Viruses in Central Nervous System. Margaret Holden, New York.—p. 88.
Bacteriologic Studies on Experimental Dental Caries in Rat: I. Bacterial Flora of Normal, Noncarious Teeth. R. W. Harrison, Chicago.—p. 91.
Id.: II. Changes in Tooth Surface Flora Associated with Development and Inhibition of Dental Caries. R. W. Harrison, Chicago.—p. 97.
Id.: III. Flora of Advanced Carious Lesions. R. W. Harrison, Chicago.—p. 106.
Sodium Azide as Inhibiting Substance for Gram-Negative Bacteria. M. L. Snyder and H. C. Lichstein, Ann Arbor, Mich.—p. 113.
Experimental Poliomyelitis in Animals Other Than the Monkey: II. Effects of Nonspecific Intracerebral Injections in Rabbits. J. A. Toomey and W. S. Takacs, Cleveland.—p. 116.
Hematology of Malaria (Plasmodium Brasilianum) in Panamanian Monkeys: I. Numerical Changes in Leukocytes. W. H. Taliaferro and Cessa Klüver, Chicago.—p. 121.
Id.: II. Morphology of Leukocytes and Origin of Monocytes and Macrophages. W. H. Taliaferro and Cessa Klüver, Chicago.—p. 162.

Journal-Lancet, Minneapolis

60:433-478 (Oct.) 1940

Preventive Allergy in Infancy and Childhood. A. V. Stoesser, Minneapolis.—p. 433.
Treatment of Common Diseases of Skin. L. A. Brunsting, Rochester, Minn.—p. 438.
Medical Observations in India. L. J. Alger, Grand Forks, N. D.—p. 442.
Early Diagnosis of Acute Appendicitis in the Preschool Child. M. Seham and A. J. Moss, Minneapolis.—p. 444.
Choice of Operation for Vesical Neck Obstruction. F. E. B. Foley, St. Paul.—p. 449.
The Physical Education Teacher as Health Counselor. T. B. Kirkpatrick, New York.—p. 451.
*Cold Prevention Studies: Abortive Treatment with Benzedrine and with Codeine-Papaverine Mixture. A. B. Baker and D. W. Cowan, Minneapolis.—p. 453.
Acute Exanthemas and Their Differential Diagnosis in the College Age Group (Colored Photography as Aid in Teaching Problems). L. R. Cole, Madison, Wis.—p. 456.
Problem of Acute Poliomyelitis. J. C. McKinley, Minneapolis.—p. 458.
*Treatment of Uncomplicated Acute Alcoholism: Preliminary Report on Effectiveness of Insulin, Glucose and Thiamine Chloride in Correcting Pathologic Physiology. G. W. Robinson Jr. and P. Shelton, Kansas City, Mo.—p. 461.

Cold Prevention Studies.—Baker and Cowan present studies on the incidence of colds among university students using amphetamine inhalers or a codeine-papaverine mixture and those employing a placebo for aborting colds at the first onset of symptoms. There were 279 students who used the amphetamine inhaler and 276 who used inhalers except that they contained no amphetamine but in appearance and odor were indistinguishable from those containing the drug. During the two years of the study the amphetamine group reported an average of 1.3 colds per person annually. This represented a reduction of 76 per cent from the average of 5.5 colds per person annually which the same students reported for the two years prior to the study. The control group reported a fall from 5.1 previous colds to 1.9 colds per person annually during the study. This represents a reduction of 63 per cent and certainly nullifies the apparent benefit given by the amphetamine inhaler. There was no difference between the two groups in number of days lost from school. The codeine-papaverine mixture was taken by 224 students and among them there was a reduction of 80 per cent in the average number of colds per person annually during the two years of the study as compared to the two previous years as compared to the reduction of 63 per cent for the control group. The results for the codeine-papaverine mixture, like those for the amphetamine inhaler, are not significantly different. An attempt to summarize the complications of the common cold which occurred during the period of the study, although the number is small, indicates that the codeine-papaverine group presented only about 50 per cent as many complications as the amphetamine group, a previously vaccinated group or the control group.

Treatment of Uncomplicated Acute Alcoholism.—For the last two and a half years Robinson and Shelton have treated their acute alcoholic patients without complicating neurosis or psychosis by correcting the metabolic disturbances by the use of insulin, intravenous dextrose, thiamine hydrochloride and a high caloric diet. One hundred and eighty-six individual patients suffering from acute alcoholism were treated by reestablishing their carbohydrate metabolism; 166 were readmitted, making a total of 352 admissions or patient procedures. Immediately after admission, 20 units of insulin is given and at the first sign of hunger liquid nourishment is provided. If the patient insists on a drink he is given one. The patient must be watched carefully and if the intensity of perspiration increases he is aroused if asleep and urged to take liquids. As an increase in perspiration is evidence of a minor insulin reaction, the patient is usually hungry and cooperative. A second dose of 20 units of insulin is given three hours after the first. This almost invariably produces hunger and the patient will take quantities of liquid food and some may take light solids. After this meal the average patient usually falls asleep and sleeps naturally for several hours. He may wake up nervous and some patients may want alcohol. Shortly after he awakens he is given 500 cc. of a 10 per cent solution of dextrose containing 10 units of insulin and 10 mg. of thiamine hydrochloride. This frequently controls all the nervous symptoms and produces complete relaxation. One or two subsequent infusions may be given if warranted. Twenty units of insulin is given at 6 and 9 p. m. of the second hospital day, and the patient usually sleeps well this night. The infusion is repeated on the third hospital day, and on this day practically all the symptoms have disappeared. The average requirement of whisky for satisfaction has been about 3 ounces (90 cc.) from admission to the disappearance of all symptoms. Convalescence from this point is uneventful. The authors base this treatment on their belief that alcoholism is a disease with a chronic progressive pathologic background characterized by successive acute pathophysiologic episodes which have primarily a nutritional background. The procedure requires careful, intelligent nursing and medical care if complications (insulin reactions, shocks) are to be minimized. The majority of the patients have liked the procedure, feeling that it has accomplished its purpose quickly and easily, as the fact that so many readmit themselves voluntarily bears out.

Journal of Pediatrics, St. Louis

17:423-570 (Oct.) 1940

*Sulfathiazole in Treatment of Pneumonia in Infants and Children: Report on 167 Patients Treated with Sulfathiazole and a Comparison with 93 Patients Treated with Sulfapyridine. J. P. Scott, Philadelphia, and A. M. Jones, Memphis, Tenn.—p. 423.
Evaluation of Enzyme Treated Milk in Infant Feeding. M. L. Blatt, E. H. Harris, H. M. Jacobs and Mary Zeldes, Chicago.—p. 435.
Prothrombin in the Newborn Infant: Relationship to Maternal Dietary Vitamin K Intake. S. Kove and H. Siegel, Brooklyn.—p. 448.
Recurrent Vomiting in Children: Factor of Food Hypersensitiveness. J. H. Fries and K. G. Jennings, Brooklyn.—p. 458.
Study of Nutritional and Physical Status and Response to Exercise of Sixteen Negro Boys 13 to 17 Years of Age. P. W. Schlutz, Minerva Morse, D. E. Cassels and L. Vivian Iob, Chicago.—p. 466.
Tuberculin Testing as Case-Finding Procedure. P. S. Phelps, V. P. Cenci and Alice Lawton, Hartford, Conn.—p. 481.
Complications of Meckel's Diverticulum in Infancy and Childhood, with Analysis of Fourteen Cases. M. W. Everhart, New Orleans.—p. 483.
Experience with Benzedrine Sulfate in Management of Obesity in Children. R. H. Kunstadter, Chicago.—p. 490.
*Duration of Diphtheria Immunity: Follow-Up Study. A. Christie, San Francisco.—p. 502.
Relation of Vitamin D Intake to the Age of the Infant at the Time of Eruption of the First Deciduous Incisor. T. D. Speidel and Genevieve Stearns, Iowa City.—p. 506.
Teratoma of Pineal Body. J. R. Gerstley, J. Kasanin and Elizabeth Lowenhaupt, Chicago.—p. 512.
Bronchiogenic Carcinoma of Seven Years' Duration in 11 Year Old Boy. M. G. Wasch, M. Lederer and B. S. Epstein, Brooklyn.—p. 521.
Health Program for the Staff of a Children's Hospital. H. H. Work Jr., East Providence, R. I.—p. 529.

Sulfathiazole for Pneumonia in Children.—Scott and Jones report on the treatment with sulfathiazole of 167 infants and children having pneumonia and on 93 treated with sulfapyridine. The usual daily sulfathiazole dose was 1 grain (0.065 Gm.) per pound of body weight. From one fourth to one half of this amount was given as an initial dose, followed by one eighth of the daily dose every three hours throughout day and night and continued until the temperature had been normal for forty-eight hours. Oxygen, transfusion, enemas, measures to combat distention and to secure a free nasal airway, incision of eardrums, aural instillations and sponging were used when indicated. Between Oct. 1, 1938, and June 1, 1939, 58 of the patients treated with sulfapyridine received daily 1½ grains (0.1 Gm.) of the drug per pound of body weight. The remaining 35 patients treated in the fall of 1939 usually received 1 grain. Sulfathiazole seemed to precipitate an early crisis similar in character to the natural crisis to that produced by specific serum or to that produced by sulfapyridine. Usually within twelve hours the fever and toxicity lessened, dyspnea was relieved and the patient began to feel better. In many cases the temperature became permanently normal in twenty-four hours. After forty-eight hours few of the patients had fever and after seventy-two hours only 19 of 158 patients successfully treated had fever. Coincident with the fall in temperature, the child's appetite improved, and activity and responsiveness returned. In a few cases listlessness did not disappear until the drug was stopped in spite of other improvement. Usually physical pulmonary signs improved when the fever abated, but great variability was noticed in this clearing, as it is after a natural crisis. Five of the patients given sulfathiazole died. In the 158 cases in which satisfactory results were obtained, the time between the beginning of treatment and the beginning of a permanent normal temperature averaged 1.8 days. Diagnosis of bronchopneumonia was made

and confirmed by roentgen examination in 18 cases, in which the average days of fever was 1.62, as compared to 1.8 days for the whole group. A study of the time elapsing between the first dose of the drug and the return of temperature to normal of the patients treated with sulfapyridine shows that one cannot infer that there is any superiority of one drug over the other in this respect. Toxic effects following sulfathiazole were largely gastrointestinal, consisting of vomiting and diarrhea, and were mild in comparison with those caused by sulfapyridine. Sulfathiazole is easy to administer to young children and infants.

Duration of Diphtheria Immunity.—Christie presents data of a follow-up study on the lasting effect of seven antigens used for diphtheria immunity. The interval between doses was only one week and the interval after immunization to Schick tests was only three months. The author realizes the discrepancies but believes that they do not minimize the lesson to be learned from an accumulation of such data. Between July 1930 and October 1931 toxin antitoxin was used on 52 children. Three 1 cc. doses of the material were given at weekly intervals. After three months Schick tests revealed that 77 per cent of the children were Schick negative. Nine of this Schick-negative group were retested nine years later and 8 were still negative. Three weekly doses of 1 cc. of toxoid to which 0.5 per cent of alum had been added and contained a flocculating unitage of from 5 to 6 units per cubic centimeter were given 49 children. In three months 93 per cent of these children were Schick negative. Fourteen of them were retested seven years later and 12 (85 per cent) were still negative. Essentially the same material, except for a higher flocculating unitage, was given in two 0.5 cc. doses to 167 children one week apart. Ninety-one per cent of these were Schick negative, while after five and one half to seven years only 52 per cent of the 44 retested were Schick negative. Between August 1932 and April 1934 plain toxoid was given to 87 children with an initial dose of 0.5 cc. followed in one week by 1 cc. After one month 87 per cent of the group had a negative Schick reaction, after five and one half to seven years 8 of the 16 retested had become Schick positive. After one dose of alum-precipitated toxoid 90 per cent of 49 children were immunized but only 46 per cent of 13 retested after five years remained so. Another preparation was given in the same manner to 101 children (one dose of 0.5 cc.) but with a flocculating unitage three and one half times that of the preceding preparation. After six weeks 95 per cent of these children were Schick negative and after four years 75 per cent of 24 negative Schick reactors retested were still negative. Two 1 cc. doses of plain toxoid one week apart produced 94 per cent negative Schick reactors among 94 children in six weeks and after four years 75 per cent of the 24 retested were still negative.

Missouri State Medical Assn. Journal, St. Louis

37:455-490 (Nov.) 1940

Coronary Vascular Disease. J. H. Musser, New Orleans.—p. 455.
Treatment of Nephritis by Rest. T. Addis, San Francisco.—p. 458.
Hyperthyroidism: Some Hazards in Surgical Treatment. E. V. Mastin, St. Louis.—p. 460.
Pneumococcic Pneumonia: Observations on Incidence and Therapy in St. Louis Area, 1939-1940. L. D. Thompson, L. L. Terry and J. C. Edwards, St. Louis.—p. 463.
Clinical Gastroscopy with Findings in 356 Examinations. B. Kenamore and H. Scheff, St. Louis.—p. 469.
Medical Care of the Old Aged Patient. C. E. Henry, Kirksville.—p. 471.
*Sulfanilamide Implantation as Method of Controlling Infection in Clean Surgical Wounds. M. A. Casberg, St. Louis.—p. 473.
Ketosis Simulating Acute Conditions of Abdomen. J. G. Probstein and N. W. Drey, St. Louis.—p. 475.
Is Dentition an Etiologic Factor in Organic as Well as Functional Derangement of Infants? C. B. Summers, Kansas City.—p. 478.
The Relationship of Physicians and Dentists. A. O. Gruebbel, Jefferson City.—p. 480.

Sulfanilamide Implantation in Clean Surgical Wounds.—Casberg used sulfanilamide crystals locally as prophylaxis against infection of clean wounds following inguinal herniorrhaphy. Two comparable groups of cases were used as controls. All the operations were performed during December, January and February, as in previous years wound infections were highest during these months. From 6 to 8 Gm. of sulfanilamide was sprinkled into the subcutaneous tissues between the skin and the aponeurosis of the external oblique muscle. There were no postoperative wound infections among the 18 patients thus treated. Two infections occurred among the 19 patients of one control group and three among 25 of another control group. Three of the infections were due to Staphylococcus aureus and 2 to Streptococcus haemolyticus. The absence of wound infection following local sulfanilamide implantation does not obviate any of the operating room rules of asepsis.

Nebraska State Medical Journal, Lincoln

25:357-392 (Oct.) 1940

Management of Ocular Trauma. T. E. Sanders, St. Louis.—p. 357.
Use of Sulfocyanates in Arterial Hypertension. G. W. Covey, Lincoln.—p. 363.
Delirium and Its Management. G. A. Young and R. H. Young, Omaha.—p. 370.
Study of 100 Sterile Marriages. L. S. McGoogan, Omaha.—p. 375.
Cancer of Tonsil. L. P. Coakley, Omaha.—p. 379.

New England Journal of Medicine, Boston

223:651-694 (Oct. 24) 1940

Observations on Epidemiology of the Common Cold. W. G. Smillie, New York.—p. 651.
Relation of Sinusitis to Chronic Nontuberculous Chest Infection. R. L. Goodale, Boston.—p. 654.
Pathogenesis of Primary and Reinfection Types of Pulmonary Tuberculosis. E. R. Long, Philadelphia.—p. 656.
Treatment of Pneumococcic Pneumonia. F. G. Blake, New Haven, Conn.—p. 661.
Osteomyelitis of Coccyx and Sacrum with Sinus Formation Simulating Anorectal Fistula: Report of Two Cases. H. E. Bacon and A. Taylor, Philadelphia.—p. 668.
Emergency Treatment of Fractures. H. C. Marble, Boston.—p. 672.

New Jersey Medical Society Journal, Trenton

37:487-528 (Oct.) 1940

Preventive Medicine in Modern Industry. E. E. Evans, Pennsgrove.—p. 492.
Lame Back. F. R. Ober, Boston.—p. 501.
Treatment of Alcoholism. M. Moore, Boston.—p. 509.

North Carolina Medical Journal, Winston-Salem

1:523-578 (Oct.) 1940

What Moves Man? J. K. Hall, Richmond, Va.—p. 523.
A Quarter-Century of Health Progress in North Carolina. R. Norton, Chapel Hill.—p. 529.
Carcinoma of Cervical Stump: Study of Incidence in a Series of Patients with Cervical Carcinoma Seen in North Carolina. R. L. Pearse, Durham.—p. 534.
Diabetes Mellitus. L. A. Crowell Jr., Lincolnton.—p. 538.
Sulfapyridine Therapy in Lobar Pneumonia, with Special Attention to Complications. E. E. McClure, G. Watson and W. R. Stanford, Durham.—p. 543.
Diagnosis and Management of Chronic Eczematoid Dermatitis of Hands. J. L. Callaway and S. W. Barefoot, Durham.—p. 547.
Experiences with Histaminase (Torantil): Preliminary Report. T. W. Baker, Charlotte.—p. 551.
Another Goiter Region. R. O. Jones, Burnsville.—p. 556.

Northwest Medicine, Seattle

39:351-392 (Oct.) 1940

*Zinc Peroxide in Treatment of Surgical Infections. J. A. Gius, Portland, Ore.—p. 354.
Obstructive Jaundice: Its Surgical Consideration. V. C. Hunt, Los Angeles.—p. 358.
Relapsing Fever. M. W. Hemingway, R. W. Hemingway and V. K. Arneson, Bend, Ore.—p. 362.
Treatment with Vitamins. D. L. Wilbur, San Francisco.—p. 364.
Education of the Acoustically Handicapped. Elvena Miller, Seattle.—p. 369.

Zinc Peroxide for Surgical Infections.—Gius reports four cases in which zinc peroxide was used with good results in three, while the fourth illustrates a hazard of introducing zinc peroxide or similar material into a closed cavity. In the first three cases the infection was localized to the parietes, but in the fourth case it was confined to the pelvis and zinc peroxide could be introduced only by injection through the colpotomy wound. The zinc peroxide suspension passed through the wall of the abscess and into the peritoneal cavity, resulting in diffuse peritonitis. Fortunately, the patient recovered and has apparently been cured.

Ohio State Medical Journal, Columbus

36:1037-1144 (Oct.) 1940

Brucellosis (Undulant Fever). W. M. Simpson, Dayton.—p. 1053.
Role of Intubation in Treatment of Intestinal Obstruction. W. O. Abbott, Philadelphia.—p. 1061.
Brief Summary of Malignant Neoplasms Proved at Autopsy Which Simulated Pulmonary Tuberculosis. R. J. Ritterhoff, Cincinnati. —p. 1066.
Eye Affections Secondary to General Diseases. E. J. Wenaas, Youngstown.—p. 1068.
Care of the Newborn. M. L. Ainsworth, Columbus.—p. 1073.
Blood Dyscrasias of Infancy and Childhood. H. Wellmeier, Piqua.—p. 1078.
Clinical Study of Intestinal Parasites. H. H. Ingling, Springfield. —p. 1083.
Consideration of Some Causes of Increased Intracranial Pressure. J. P. Evans, Cincinnati.—p. 1086.
Splenomegaly and Hepatic Enlargement Apparently Relieved by Injections of Spleen Fluid: Report of Case. G. A. Hoke, Elyria.—p. 1090.
Some Errors and Misconceptions in Clinical Endocrinology. A. G. Sar-Louis, Cleveland.—p. 1092.
Acute Chest Conditions in Children. W. B. Taggart, Dayton.—p. 1096.

36:1145-1248 (Nov.) 1940

Facts and Fiction About Our State Hospitals. W. Overholser, Washington, D. C.—p. 1161.
Diagnosis and Significance of Tuberculous Infection. J. H. Skavlem, Cincinnati.—p. 1168.
Minor Discomforts of Pregnancy. F. W. Davis, Columbus.—p. 1174.
Vaginopelvic Massage and Tamponade: Conservative Gynecologic Procedure. C. J. Vogt, Cleveland.—p. 1178.
Symmetrical Cerebral Calcification Simulating Brain Tumor. A. T. Steegmann, Cleveland.—p. 1181.
Acute Respiratory Emergencies. S. C. Yinger, Springfield.—p. 1185.
Ophthalmoscopic Interpretation of Retinal Vascular Disease. W. F. Hatcher, Youngstown.—p. 1190.
Urban Safeguards Against Milk-Borne Diseases. H. J. Knapp, Cleveland.—p. 1191.
Roentgen Kymography in Study of the Heart in Childhood. J. V. Greenebaum, S. Brown and T. Selkirk, Cincinnati.—p. 1194.
Acute Cholecystitis. R. C. Austin, Dayton.—p. 1198.
Immediately Preoperative, Fatal Pulmonary Embolus. R. R. Renner and K. S. Russell, Cleveland.—p. 1201.

Pennsylvania Medical Journal, Harrisburg

44:1-128 (Oct.) 1940

Lest We Forget: Presidential Address. F. F. Borzell, Philadelphia.—p. 13.
*Clinical Report of Epidemic of Acute Infectious Jaundice. B. G. Learn, Blandburg.—p. 18.
Spontaneous Expulsion of Submucous Lipoma of Cecum. G. S. Backenstoe, Emmaus.—p. 21.
The Hospital's Personality and Environment. B. Gordon, Philadelphia. —p. 23.
Role of Infection in Kidney Disease. J. A. Kolmer, Philadelphia.—p. 26.
Subtotal Gastrectomy for Peptic Ulcer. W. T. Lemmon, Philadelphia.—p. 31.
Chronic Adult Tetany of Gastrointestinal Origin: Treatment with Dihydrotachysterol: Report of Case. V. W. Eisenstein, Pittsburgh. —p. 33.
Treatment of Tetany with Dihydrotachysterol. T. C. Wilkinson, Pittsburgh.—p. 37.
Diabetes: VI. Diabetic Diets and Eating Habits of Nationalities. A. L. Luchi, Wilkes-Barre.—p. 41.
Indirect Blood Transfusion: Simplified Method: Report of 196 Cases. S. A. Rosenburg and H. J. Bayer, Pittsburgh.—p. 45.
Staphylococcic Septicemia Coexisting with Diabetes: Report of Case with Recovery. H. H. Seiple, Lancaster.—p. 50.

Epidemic of Acute Infectious Jaundice.—Learn discusses sixty-two instances of epidemic acute infectious jaundice encountered in his private practice. The cases began to appear in September 1937 and continued to March 1938; no more cases were observed until September 1938, when the epidemic again became prevalent and lasted until March 1939. Since that time only three cases have been observed. Most of these cases were mild and ambulatory; the greatest number occurred in children from 6 to 8 years of age. The youngest patient was 3 and the oldest 47 years of age. The severity of the illness usually increased with the age of the patient. The incubation period was two weeks in most of the cases. As many as six cases occurred in one family, but not all the exposed children were affected. Clinical evidence shows that the disease is transmitted from person to person and that most adults are immune. There were few complications and only one death in the author's series. Epigastric pain, nausea, fever and tenderness in the upper right quadrant occurred in all the cases, vomiting in forty-seven, bile in the urine in thirty-six cases, clay-colored stools in eighteen and epistaxis in twelve. A spirochete which resembles Leptospira was isolated in a sufficient number of the cases to determine that it was the cause of the epidemic. In two of the three cases in which there was a recurrence of the jaundice the darkfield examination was positive. In one of these the spirochetes were recovered from the macerated kidney substance of an inoculated guinea pig.

Public Health Reports, Washington, D. C.

55:1879-1932 (Oct. 18) 1940

Housing Problem as It Affects Public Health Nursing Activities. Mary J. Dunn.—p. 1879.
Sanitary and Physiologic Aspects of Flooring Materials. J. M. DallaValle.—p. 1884.
Studies on Duration of Disabling Sickness: I. Duration of Disability from Sickness and Nonindustrial Injuries Among the Male and Female Memberships of Twenty-Five Industrial Sick Benefit Organizations, 1935-1937, Inclusive. W. M. Gafafer and Elizabeth S. Frasier.—p. 1892.
Rheumatic Fever in New Haven, Conn.: Survey of Recent Hospital Admissions. Lucille R. Farquhar and J. R. Paul.—p. 1903.

55:1933-1976 (Oct. 25) 1940

*Institutional Outbreak of Pneumonitis: I. Epidemiologic and Clinical Studies. J. W. Hornibrook and K. R. Nelson.—p. 1936.
*Id.: II. Isolation and Identification of Causative Agents. R. E. Dyer, N. H. Topping and I. A. Bengtson.—p. 1945.
*Relation of Body Build to Drug Addiction. R. R. Brown.—p. 1954.

Institutional Outbreak of Pneumonitis.—According to Hornibrook and Nelson, 15 cases of pneumonitis occurred during the spring of 1940 among the 153 employees in one building of the National Institute of Health. The roentgenograms of the cases showed one or more pneumonic shadows. There were a few other cases of a somewhat similar but milder type which gave no roentgen signs or roentgenograms were not obtained. The onset was fairly sudden though usually not severe. Two types of onset predominated, one coryza-like, the other with headache, chilly sensations and general malaise. There was a latent period of about three days following the onset in which the patient continued to work although feeling ill. Severe and persistent headache was a prominent symptom developing during the latent period. In none of the cases was a "prune juice," rusty or blood-tinged sputum observed. Approximately half of the patients developed vague neuralgic chest pains in the substernal region or on the side of their demonstrated pulmonary lesion. All the patients complained of insomnia. There were no physical abnormalities on physical examination; in fact, their absence was one of the characteristics of the disease. On admission the average pulse rate was 99 beats and the average temperature was 102.4 F. (varying from 100.5 to 104.5 F.). The pulse rate did not always parallel the temperature curve. The roentgen examination gave the most typical and consistent evidence of pulmonary lesions. A soft infiltrative lesion, single or multiple, was visible on the films but was not of the uniform density seen in lobar pneumonia. The lesions appeared to be more of the patchy type seen in bronchopneumonia. It is doubtful whether many of the patients would have been considered as having a pneumonic process without roentgen examination. Blood cultures, agglutination tests, using Eberthella typhi, Brucella abortus, Bacillus proteus OX19 and Pasteurella tularense as antigens, and sputum studies for pneumococci were negative. The usual supportive hospital treatment was given all the patients. Other than 1 death there were no serious complications. Dyer and his co-workers isolated the etiologic organism, the rickettsia of Q fever, from 3 of 4 of the epidemic cases in which it was attempted. From various reports by other workers it seems possible that this disease has had a widespread geographic distribution; the cases of these other outbreaks have been reported as bronchopneumonia of unknown etiology (variety X), atypical pneumonia and atypical bronchopneumonia. The clinical course of these outbreaks and of the epidemic under discussion was consistent. The three strains isolated gave cross immunity to one another, to strain of American Q fever previously reported from the laboratory of the National Institute of Health as "strain X" and to a strain of Australian Q fever received from Burnet. Dyer and his co-workers point out that no valid evidence was adduced that personal contact or the intervention of an arthropod vector was responsible for the transmission of the disease. Strains of Q fever have been carried in animals and tissue cultures in one unit of the National Institute of Health since 1938. Whether or not this unit served as a source of infection is open to question, since the personnel of the unit was spared and the cases were widely distributed throughout the building.

Body Build and Drug Addiction.—Brown made anthropometric studies of 400 native white male adult addicts following their admission to the United States Penitentiary Annex, Fort Leavenworth, Kansas. The cases represented consecutive admissions, the only selecting factors being those of color, nativity and verified history of drug usage. Measurements were taken on unclothed patients according to the technic of Hrdlicka. Subjective estimates were made also of the face shape, face profile, conformation of head, baldness, neck, trunk profile, general appearance as to nutrition, skin color, musculature, dysplastic traits and estimate of body type. On the basis of the investigation the narcotic drug addicts of the study were average or slightly superior in height and weight. There was an average gain in weight of a little more than 3 Kg. (6½ pounds) after five and a half months of institutionalization. The body build of the group was found to be within normal limits with a trend toward the pyknic end of the distribution. The drug addiction of the group could not be ascribed to gross constitutional weakness.

Southwestern Medicine, El Paso, Texas

24:319-356 (Oct.) 1940

Cancer of Small and of Large Intestines. J. S. Horsley, Richmond, Va.—p. 319.
*Necessity for Accuracy and Simplification in Diagnosis of Renal Tuberculosis. J. L. Emmett, Rochester, Minn.—p. 324.
Relation of Psychiatry to Other Departments of Medical Practice. S. D. Ingham, Los Angeles.—p. 331.
Bronchial Obstruction. T. H. Bate, Phoenix, Ariz.—p. 336.
Retention Catheter Treatment of Vesicovaginal Fistula. R. F. Thompson, El Paso, Texas.—p. 338.
Abdominal Surgical Emergencies. E. P. Palmer, Phoenix, Ariz.—p. 340.

Diagnosis of Renal Tuberculosis.—Emmett points out that in the diagnosis of renal tuberculosis the trend is away from retrograde pyelography and toward excretory urography. There are only four methods of investigating a kidney in the presence of tuberculous disease, and all may give negative results even though tuberculosis is present. These methods are urography, determination of pus corpuscles in a "wet smear" of urine obtained by ureteral catheterization, microscopic examination of a stained specimen of ureteral urine for acid-fast bacilli, and inoculation of guinea pigs with a catheterized specimen of urine. All these examinations except descending urography require cystoscopic investigation. More than one cystoscopy may be required to make all of them. Cystoscopy carried out in the presence of urinary tuberculosis is usually a painful procedure unless anesthesia is employed. Repeated cystoscopy is not only painful but it may traumatize infected tissue. Only those examinations should be employed which enable one to arrive at a sound diagnosis. The ultimate in diagnosis in renal tuberculosis is the minimal amount of investigation that will permit a diagnosis sufficiently accurate to suggest correct treatment. One brief cystoscopic examination should be sufficient in each case. Repeated instrumentation is to be avoided. The excretory urogram will indicate the involved kidney in most cases and it is accurate in this regard. The excretory urogram will suggest the condition of the uninvolved kidney, but this information is inaccurate and must be supplemented by an examination of a ureteral specimen of urine, by microscopic examination of the wet smear, special staining methods for acid-fast organisms and inoculation of guinea pigs with specimens of urine. Retrograde pyelography is rarely necessary for the involved kidney but is occasionally necessary for the uninvolved kidney when the excretory urogram is poor. Routine bilateral pyelograms are entirely unnecessary and are not in the interest of the patient either economically or physically. They may be necessary in a small group of cases in which the diagnosis is in doubt. The results of nephrectomy in 1,131 cases of renal tuberculosis performed at the clinic between 1912 and 1932 indicate that the term "unilateral" renal tuberculosis is not justified. They demonstrate that the more nearly "normal" the uninvolved or the least involved kidney is proved to be, the better will be the clinical results following removal of the involved kidney. The results of nephrectomy in grossly bilateral renal tuberculosis are not good and do not justify its performance on the belief that removal of the worse kidney may relieve the vesical symptoms. Of 718 cases in which the specimen of urine from the uninvolved kidney contained no pus corpuscles, 65.2 per cent of the patients were either cured or improved at the end of five years and 56.4 per cent at the end of ten years. Among these cases there were 55 in which inoculation of guinea pigs with urine gave positive results, and only 36.4 per cent of these patients were cured or improved at the end of five years and only 30 per cent were alive at the end of ten years. The best results were obtained among 209 patients in whom no pus corpuscles were being excreted from the uninvolved kidney and the results of inoculation of animals with specimens of ureteral urine were negative. At the end of five years 75.2 per cent of the patients were cured or improved and at the end of ten years the percentage was 65.5.

Surgery, Gynecology and Obstetrics, Chicago

71:569-696 (Nov.) 1940

*Blood and Lymph Vessel Tumors: Report of 1,056 Cases. W. L. Watson and W. D. McCarthy, New York.—p. 569.
*Acute Intestinal Obstruction. C. W. Mayo, J. M. Miller and L. K. Stalker, Rochester, Minn.—p. 589.
Reaction of Bone to Multiple Metallic Implants. R. T. Bothe, L. E. Beaton and H. A. Davenport, Chicago.—p. 598.
*Ivy Bleeding Time, Serum Volume Index and Prothrombin Content of Blood in Estimating Bleeding Tendency in Jaundice. L. K. Ferguson, D. G. Calder Jr. and J. G. Reinhold, Philadelphia.—p. 603.
Perforated Peptic Ulcer: More Accurate Method of Roentgen Diagnosis. A. J. Williams and H. V. Hartzell, San Francisco.—p. 606.
Pregnancy and Experimental Pulmonary Tuberculosis in Rabbits. H. E. Burke, Ray Brook, N. Y.—p. 615.
Pharmacodynamic Effects of Certain Oxytocics on Tubal Contractions in Rhesus Monkey. A. H. Morse, New Haven, Conn., and I. C. Rubin, New York.—p. 620.
Resection of Portion of Thoracic Esophagus for Carcinoma: Report of Two Cases. B. N. Carter, Cincinnati.—p. 624.
Head Injury Survey. H. V. Briesen, Los Angeles.—p. 633.
Fractures in Region of Elbow in Children: End-Result Study. A. H. Brewster and M. Karp, Boston.—p. 643.
Multiple Primary Carcinoma. O. F. Lamson, Seattle.—p. 650.
Essential Problems in Surgical Treatment of Inguinal Hernia. L. M. Zimmerman, Chicago.—p. 654.
Treatment of Cervical Nodes in Intra-Oral Cancer. J. J. Duffy, New York.—p. 664.
Extraperitoneal Method of Repairing Third Degree Prolapse of Sigmoid Following Colostomy. J. R. Veal, Washington, D. C.—p. 672.
Gas Cysts of Intestine. J. A. Jackson, Madison, Wis.—p. 675.
Injury to Femoral Articular Cartilage by Medial Meniscus. A. deF. Smith and B. B. King, New York.—p. 679.

Blood and Lymph Vessel Tumors.—Watson and McCarthy made a study of 1,056 patients with 1,363 benign lymph and blood vessel tumors admitted to the Memorial Hospital during 1931 to 1939. There were 1,308 hemangiomas, 41 lymphangiomas and 14 hygromas. Seventy-three per cent of the patients presented evidence of tumor at birth and 85 per cent developed before the end of the first year. The authors propose a classification based on clinical, pathologic and therapeutic considerations: capillary hemangioma, cavernous hemangioma, angioblastic or hypertrophic hemangioma, racemose hemangioma, diffuse systemic hemangioma, metastasizing hemangioma, naevus vinosus or port wine stain, and hereditary hemorrhagic telangiectasis (Rendu-Osler-Weber disease). Solid carbon dioxide was satisfactory for superficial capillary lesions and for clearing the residual mottled areas remaining after sodium morrhuate therapy. Sodium morrhuate injection was most effective for simple cavernous and stellate hemangiomas and for Rendu-Osler-Weber disease. Solid carbon dioxide and sodium morrhuate were used together or combined with radiation. External radium brass applicators were especially applicable for capillary hemangiomas that were too thick for solid carbon dioxide therapy and also for superficial small cavernous hemangiomas resistant to sodium morrhuate. Interstitial irradiation, radon-filled, hollow 4 mm. gold seeds, was reserved for the most resistant hemangiomas and was especially well adapted for thick, bulky capillary or cavernous hemangiomas requiring skin damaging doses of external radiation. Gold radon seeds were employed for rapidly growing hemangiomas resistant to sodium morrhuate and as an adjunct for racemose angiomas. The end results obtained with high, medium and low voltage roentgen rays were disappointing. However, high voltage roentgen therapy seems indicated for osseous, large hepatic cavernous hemangiomas, hemangiomas of joints, synovia, inoperable extensive muscle angiomas and certain racemose hemangiomas. There is no successful treatment for metastasizing hemangioma. More good regressions were obtained in infants less than 3 months of age than in those more than 6 months of age. Radiation measures are hazardous and should be used with caution for hemangio-

mas of the scalp, midline areas over the sternum or vertebrae, breasts, genitalia, long bones, lips and areas adjacent to the eyes. Surgical excision is indicated for the small papillar tumors, bulky capillary lesions in areas where scars may be concealed, the resistant angiolipomas, muscle hemangiomas and angiofibromas. Port wine stains do not respond well to radiation, solid carbon dioxide or sodium morrhuate. Small lesions may be excised, but larger ones can be improved cosmetically only by covering them with cosmetic paste. The percentage of good results for surgical excision was 91, for solid carbon dioxide 88, for sodium morrhuate 86, for a combination of the latter two measures 86, for combined radiation and physical methods 65, for external radon radiation 61, for interstitial radon radiation 59, for "x-radiation" 48 and for combined radiation 57. Lymphangiomas, like hemangiomas, may possess marked growth capacity and are not, as was once supposed, dilated, static, normal lymph channels. Of the 41 lymphangiomas 61 per cent were present at birth and 95 per cent were observed before the age of 10. The lymphangiomas have been classified into five divisions: simple, cavernous, cellular or hypertrophic, diffuse systemic lymphangiomas and cystic hygroma or the cystic lymphangioma. The tumor definitely develops from lymphatic tissue in the neck, axilla, retroperitoneal tissues or groin. Hygromas are generally present at birth and grow rapidly. Thirteen of the 14 tumors were located in the neck and the other one in the axilla. Wide surgical excision affords the best prognosis in the treatment of lymphangiomas despite unsightly scars and postoperative keloids. The operative results were good in 77 per cent of 13 patients. Lymphangiomas are radioresistant. However, irradiation is the method for diffuse systemic lymphangiomas which affect an entire extremity. Sodium morrhuate injections have no effect on lymphangioma, with the exception of cystic hygroma. Seventeen lymphangiomas recurred. Cystic lymphangiomas (hygromas) are relatively radioresistant. Surgical excision was performed in 7 cases with a good result in 5. Sodium morrhuate should be tried for all hygromas and if it fails, surgical excision should be tried, and if excision is incomplete then irradiation may be attempted.

Acute Intestinal Obstruction.—Mayo and his associates point out that the mortality from acute intestinal obstruction continues despite improvements in surgical technic and added therapeutic aids. Bands and adhesions, congenital or inflammatory, are second only to external hernias as causes of intestinal obstruction. Twenty-four patients suffering from acute intestinal obstruction as a result of bands and adhesions were seen at the Mayo Clinic from 1935 to 1939, during which time 136 cases of acute intestinal obstruction were encountered. Of these 136 cases 81 were due to external hernias. Internal hernias as a result of abdominal operations are less frequent, owing to operative precautions, such as the suturing of the stomach to the opening in the transverse mesocolon when posterior gastro-enterostomy is performed. The more important internal hernias at present are those resulting from congenital defects. Seven cases of internal hernias and acute intestinal obstruction were seen at the clinic during the five years under consideration. Volvulus of various portions of the intestinal tract accounted for only 9 acute intestinal obstructions. Intussusception accounted for 10 cases; 8 of the patients were 2 or less years of age, 1 was 4 and 1 was 6. Three of the cases were caused by mesenteric thrombosis, 2 were due to gallstones, 2 to congenital mesenteric cysts, 2 to diverticulitis and 4 to carcinoma. Simple mechanical obstructions of the small intestine early in the postoperative period in which strangulating lesions can be eliminated respond well to decompression of the intestine by the Wangensteen method. This is not true for obstructions of the small intestine caused by bands and adhesions in the late postoperative period. Analysis of the results of this group reveals a high incidence of strangulation. Signs indicative of strangulation must be watched for and, if not present, conservative treatment may be employed. Colonic obstruction must be considered a strict contraindication to the use of suction drainage. Cecostomy or colostomy is the procedure of choice and does not carry an elevated risk in comparison with "blind" intubation. When operation is indicated, the most conservative procedure possible under the existing circumstances should be employed after the patient has been properly prepared. When resection is necessary, the loop should be exteriorized and the continuity of the intestine restored later when the patient is in better condition. Primary resection with closure of the intestine and side to side anastomosis is too hazardous a procedure unless performed for a small lesion high in the intestine. Useful postoperative therapeutic adjuncts are blood transfusions and 100 per cent oxygen. There is a correlation between the duration of obstruction or strangulation and the mortality rate. The combined mortality among the 136 patients was 22 per cent and of the patients who died about half had been ill for more than forty-eight hours before coming to operation and an additional 3 had been ill about forty-eight hours. The adverse effect of delay in recognizing and treating strangulating lesions is especially true in obstructions caused by bands and adhesions in the late postoperative period. The prophylactic repair of hernias in suitable cases will reduce not only the incidence of obstruction but also the resultant mortality rate.

Tests Estimating Bleeding Tendency in Jaundice.—Ferguson and his associates performed simultaneously the Ivy bleeding time test, the serum volume test of Boyce and McFetridge and the Quick method of determining the prothrombin content of the blood. The estimations were made from the same specimen of blood drawn from each of 27 jaundiced patients. The jaundice was due to various causes. The authors find that there is sufficient correlation between the tests to warrant confidence in the use of the two simpler tests as adjuncts to or substitutes for prothrombin studies or when laboratory facilities for prothrombin determination are not available. A blood prothrombin level of 30 per cent or less was selected arbitrarily as a level at which danger of bleeding due to prothrombin lack was imminent. Of nine determinations in which the prothrombin percentage was 30 per cent or less either the Ivy bleeding time or the serum volume index or both indicated a definite bleeding tendency. In 2 cases in which the prothrombin percentage was respectively 33 and 50 per cent, a definite hemorrhagic tendency was suggested by the Ivy bleeding test, the serum volume index and clinical evidence of bleeding. In a third case with a prothrombin determination of 30 the serum volume index was 0.76, not indicative of a bleeding tendency, though the Ivy bleeding time was ten minutes. In none of the cases with a prothrombin percentage above 30 was there clinical evidence of bleeding. Seven of these patients showed a serum volume index between 0.7 and 0.8 and in 3 of these the Ivy bleeding time indicated a bleeding tendency and in 1 the serum volume index was reduced to a definitely critical level. However, in no case did both tests indicate a definite hemorrhagic tendency, although in 2 with the Ivy bleeding time prolonged the serum volume index was between 0.7 and 0.8. Therefore either one or both of the two simple tests showed the tendency to hemorrhage in cases in which it was indicated by the blood prothrombin level. In 2 cases both tests indicated the hemorrhagic tendency in agreement with the clinical evidence, while the prothrombin percentage did not. In 4 cases one or the other of the simpler tests indicated a hemorrhagic tendency when there was no other evidence that it existed.

Texas State Journal of Medicine, Fort Worth

36:401-462 (Oct.) 1940

Anemias of the Newborn Period. B. Reading, Galveston.—p. 405.
Effect of Drugs on Hematopoietic System. M. D. Levy, Houston.—p. 410.
Biochemical Aspects of Hematology. M. Bodansky, Galveston.—p. 415.
X-Ray Treatment of Ewing's Tumor. R. H. Crockett, San Antonio.—p. 417.
Roentgen Diagnosis of Calcified Pelvic Tumors. C. A. Stevenson, Temple.—p. 422.
Some Epithelial Tumors of Eyelids and Their Management. S. K. Stroud and C. D. Stewart, Corpus Christi.—p. 426.
Anesthesia in Peroral Endoscopy. J. B. Nail, Wichita Falls.—p. 430.
Hyoid Bursitis. L. A. Nelson, Dallas.—p. 435.
Endocrine Factor in Dysfunction of Organs of Special Sense. H. L. Warwick, Fort Worth.—p. 438.
Activities of the Bureau of Food and Drugs of the Texas State Department of Health. F. D. Brock, Austin.—p. 440.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Edinburgh Medical Journal

47:645-716 (Oct.) 1940

Role of Zinc Ionization in Treatment of Allergy in Nose. J. F. Birrell.—p. 645.
Contributions of Genetics to Reconstructive Medicine. F. A. E. Crew.—p. 653.
Gas Warfare. J. Kendall.—p. 664.
Study on Allergy in Experimental Tuberculosis. C. Clayson.—p. 675.
Artificial Pneumoperitoneum Applied to Certain Therapeutic Problems in Pulmonary Tuberculosis. J. P. McIntyre.—p. 687.
Expectorants in Chronic Bronchitis. S. Alstead.—p. 693.
*Action of Acetylsalicylic Acid on Teeth. D. B. Dott.—p. 700.

Action of Acetylsalicylic Acid on Teeth.—Dott found that strong solutions of acetylsalicylic acid extract calcium from teeth. His observations leading to this observation were as follows: He dissolved 5 grains (0.32 Gm.) of acetylsalicylic acid in 1 ounce of distilled water at about 140 F. The solution was poured on four teeth in a 2 ounce bottle. This was gently rotated and the solution was quickly filtered after five minutes, and then ammonia and ammonium oxalate were added. There was an immediate white cloudiness soon settling as a definite precipitate. The teeth used appeared normal and free from carious matter. The experiment was repeated and the solution was left in contact with the teeth for ninety minutes before filtering and precipitating. The washed oxalate was dried and strongly ignited in a porcelain crucible, and the resulting calcium oxide weighed 0.011 Gm. (0.17 grain). In several other experiments it was found that the loss of weight of the teeth after the action of acetylsalicylic acid was much greater than the weight of calcium oxide obtained. By dissolving equal weights of acetylsalicylic acid and sodium bicarbonate, one obtains a faintly alkaline solution which has no appreciable action on teeth. The author points out that the question as to how far these facts should limit the use of acetylsalicylic acid as a mouth wash is for medical decision.

Glasgow Medical Journal

16:115-146 (Oct.) 1940

Analogy Between Intrinsic Muscles of Eye and Muscle of Heart. A. M. Ramsay.—p. 115.
Codeine in Chronic Bronchitis. S. Alstead.—p. 126.

Guy's Hospital Gazette, London

54:281-298 (Oct. 5) 1940

*Cerebrospinal Meningitis. N. Mutch.—p. 282.
*Insulin Substitutes—Résumé of Present Day Knowledge. G. R. W. N. Lantz.—p. 285.
Notes on Peripheral Nerve Injuries. R. H. Harley.—p. 288.
*Strangulated Inguinal Hernia in Child of 5 Weeks. J. Gordon.—p. 290.

Cerebrospinal Meningitis.—The only effective prophylaxis, according to Mutch, against cerebrospinal meningitis consists in free ventilation and the avoidance of overcrowding. Since the survival time of the isolated meningococcus is short, the disease can be contracted only by close association with some one already infected. It was found that the carrier rate of infection could be reduced in dormitories to 5 per cent by spacing beds 3 feet apart, compared with a 20 per cent rate in 1 foot bed interspacing and a 29 per cent rate in a 9 inch bed interspacing. In the treatment of cerebrospinal meningitis, lumbar puncture and antimeningococcus serum have been replaced by sulfanilamide and sulfapyridine with marked results. Here the superiority of one drug over the other has not yet been determined. In 5,306 cases notified during the war years of 1914-1918 mortality was as high as 65 per cent; in 5,093 cases reported for the first six months of 1940 the death rate was only 20 per cent. Lumbar puncture is performed only at weekly intervals or when definite signs of increased intracranial pressure are observed. The dosage, administered in approximately equal quantities for the two drugs, ranged from 3 Gm. in infants to 9 Gm. in adults (down to 15 years) and was given daily for a week in six doses spaced four hours apart in order to maintain a uniform concentration in the body tissues but allowed for adjustments in severe attacks with supplementary intravenous injections of soluble sulfapyridine. Comatose patients were given the drug in powdered form in suspension through a stomach tube. Intramuscular injections were found impracticable for a number of reasons. In view of the frequent occurrence of adrenal hemorrhage in cases of septicemia rapidly terminating fatally, vitamin C, citrus fruits and adrenal cortex extract are tentatively suggested as means of saving life. Since rapid dehydration occurs in unconscious pyrexial patients, a copious fluid intake is recommended either by stomach or by rectal tube or by an intravenous drip of dextrose-saline solution. The author discusses the nature of the infective organism, its path of invasion, the spread of the infection, the clinical varieties of the disease and complications such as the common occurrence of arthritis. A preparation that is inexpensive, soluble and susceptible of being administered rectally to unconscious patients or to those with troublesome cerebral vomiting is a desideratum.

Insulin Substitutes.—Luntz summarizes present day knowledge of insulin substitutes. All of these aim at curing or alleviating diabetes by oral administration. However, no remedy replacing insulin for pancreatic dysfunction has yet been found. The use of substitutes not only delays initiation of proper medication but invites the progress of the disease to a dangerous stage. Improvement attributed to the oral use of substitutes is, in reality, due to the strict regimen imposed on the patient, as various investigations have shown. Substances employed as substitutes or experimented with include guanidine derivatives, succinic acid, a decoction of the kadal ranji root, a hypoglycemic extract of the roots of the "devil's club," duodenal extracts, vegetable protein preparations, protein injections and cabbage extracts. Guanidine derivatives are synthetic compounds with an effect resembling that of insulin. Used on the continent they have been found by British investigators to be impracticable and even dangerous. A continental product (synthalin), a decamethylene diguanidine hydrochloride and reported to lower blood sugar, did in some cases lower ketosis in the urine but also exhibited toxic properties by inducing gastrointestinal disturbances in many patients and jaundice and hepatitis in others. Synthalin is a harmful drug, as it lowers the blood sugar not by promoting increased oxidation of dextrose but by a toxic effect on the liver. Neosynthalin, containing fourteen methylene groups, appears to be less toxic and perhaps not so active as the original product. Succinic acid, orally administered for the control of diabetic ketosis, in the hands of English and Scotch analysts either gave negative results or failed to prevent the onset of diabetic coma or to diminish chronic diabetic ketonuria. Györgyi, its author, proceeded on the assumption that the C_4 carboxylic acids, especially pyruvic acid, played a vital part in intermediate carbohydrate metabolism and that ketosis represented a dysfunction of these acids and could be prevented by succinic acid (obtained from amber, $COOH.CH_2.CH_2.COOH$, containing four carbon atoms) acting as a catalyzer. The kadal ranji root decoction popularly used by Indians for diabetes, renders the urine of diabetic subjects sugar free by raising the renal threshold for the excretion of sugar. It is considered dangerous by its author. Investigations of the hypoglycemic substance inherent in the extracts from the devil's club root (Fatasia horrida) and ostensibly nontoxic is being further investigated. Duodenal extracts, first used in 1939, failed to give uniform clinical results. The extract varied in different cases, not in relation to the actual severity of the case, but rather to the duration of the disease. A diminution of hyperglycemia, glycosuria and diuresis and an increase in weight were noted. A vegetable protein preparation derived from the germ of the carob or locust bean (Ceratonia siliqua) and tried out on diabetic children yielded inconclusive results. Protein injections prepared by G. Singer merit further consideration, though his view that they form the basic treatment of diabetes cannot be accepted. The mechanism of action is by no means clearly understood. The effect on diabetes may be due to their power of modifying metabolism. Experiments with cabbage extracts on blood sugar concentration, with which MacDonald and Wislicki experimented on animals, chiefly rabbits, to discover a preparation devoid of toxic effects, yielded them both a hyperglycemic and a hypoglycemic fraction. The latter was effective orally as well as when injected and no hypoglycemic convulsions

were evoked. In a depancreatized dog which had been kept alive by injections of insulin, blood sugar and glycosuria were controlled by the sole use of this extract and insulin could be withdrawn entirely. A two day interval between withdrawal of the cabbage extract and resumption of insulin therapy was marked by an abrupt rise in the concentration of dextrose in the blood and urine. According to Luntz the specificity of insulin in the successful management of diabetes should constantly be emphasized against the proponents of all irrational medicines and therapies until a better remedy has been found. Synthetic products so far evolved cannot compare with insulin in efficacy and are of little if any use in the practical treatment of diabetes. The ultimate conquest of diabetes may depend on a more thorough understanding of carbohydrate metabolism. That implies a better understanding of the anterior pituitary, the adrenal cortex and various other active agents in the body.

Strangulated Inguinal Hernia in Infant.—Gordon reports the rare case of strangulation of congenital hernia in an infant aged 5 weeks, the third child born of a normal mother aged 26. At birth the mother had noticed a lump in the right groin, which, however, had disappeared a week later. The reappearance of this lump under circumstances of aggravated screams, bile-stained vomiting and attacks of colic caused the child to be hospitalized. The lump was found to be red, tense and irreducible. No right testis was found. The abdomen was distended with visible coils of intestine but with no visible peristalsis. There were no feces in the rectum. When the inguinal canal was opened a tense hernial sac was encountered, containing about 8 inches of blue ileum, 1 inch of which was plum colored. A tough constriction of the internal inguinal ring was divided, but as the child began to cry no resection of the intestine was attempted and no repair operation done to strengthen the inguinal sac. The child was given 20 ounces (600 cc.) of saline solution by subcutaneous drip during the first twelve hours after the operation and was then breast fed. The child continued to feed normally, no longer vomited, recovered stool action and was discharged six days later.

Journal of Hygiene, London

40:501-614 (Sept.) 1940

Somatic Antigens of Clostridium Welchii Group of Organisms. D. W. Henderson.—p. 501.
Design and Significance of Synergic Action Tests. K. Mather.—p. 513.
Bismuth Sulfite Mediums for Isolation of Vibrio Cholerae. W. J. Wilson and L. V. Reilly.—p. 532.
Inheritance of Resistance, Demonstrated by Development of Strain of Mice Resistant to Experimental Inoculation with Bacterial Endotoxin. A. B. Hill, J. M. Hatswell and W. W. C. Topley.—p. 538.
Osmotic Pressure, After Resolution, of Serum Dried from Frozen State (F. D. Serum). G. S. Adair, Muriel E. Adair and R. I. N. Greaves.—p. 548.
Poisoning by 2-Methylbutyraldehyde (Isovaleraldehyde). J. F. Wilkinson.—p. 555.
Use of Hypochlorites for Aerial Disinfection. A. H. Baker, S. R. Finn and C. C. Twort.—p. 560.
Effects of Morphine, Diacetylmorphine and Some Related Alkaloids on Alimentary Tract: Part V. Discussion on Probable Mechanism of Constipating Action of Morphine. G. N. Myers.—p. 583.
Chemotherapy in Cerebrospinal Meningitis in the Sudan. R. M. Buchanan.—p. 605.

Lancet, London

2:443-474 (Oct. 12) 1940

Experience at Casualty Clearing Station. J. J. M. Brown, W. M. Dennison, J. A. Ross and D. Divine.—p. 443.
*Radiography in Postoperative Ileus. P. B. Ascroft and E. Samuel.—p. 445.
Treatment of Pneumonia with Sulfapyridine and Serum. T. Anderson and J. G. Cairns.—p. 449.
*Sulfathiazole in Treatment of Pneumococcic Lobar Pneumonia. W. F. Gaisford and W. Whitelaw.—p. 451.
Toxic Manifestations of Calcium Therapy in Heart Failure. A. S. Rogen.—p. 452.

Roentgenography in Postoperative Ileus.—Ascroft and Samuel report a study of radiologic diagnosis of intestinal obstruction. Of 75 cases treated, 18 belong to the postoperative group; in most there was peritonitis, and symptoms developed of the type of ileus usually called paralytic. The plain roentgenograms were a great help in assessing individual cases. Whenever the abdomen is opened, the motility of the gastrointestinal tract and, to a lesser extent, its secretory and absorptive capacity are disturbed, producing adynamic ileus. This condition is nearly always transient, subsiding in from six to twelve hours, and needs no special treatment; but, when there is peritonitis, especially if it is due to bacteria, adynamic ileus persists, and the abdomen may become greatly distended. All the signs of intestinal obstruction are present save one: there is no peristalsis. This makes diagnosis easy and obviates an attempt to relieve an "obstruction" by operation. The same applies to the rare instances of severe and persistent adynamic ileus uncomplicated by peritonitis. However, most cases causing anxiety after operation are not of this type. The authors show that most cases of postoperative ileus causing anxiety are due either to focal obstruction at the line of suture or, more commonly, a diffuse or peritonitic obstruction. Plain roentgenograms give evidence of obstruction in both types of case. In 5 cases of suspected focal obstruction, roentgenography excluded obstruction, no operation was performed and recovery occurred. In 9 cases of peritonitic obstruction, roentgenography demonstrated obstruction of the small intestine. In cases of obstruction, plain roentgenograms taken in the erect position show distention of the small bowel with fluid levels in the distended loops. In cases not requiring immediate operation intestinal drainage by suction through a duodenal or Miller-Abbott tube should be combined with serial roentgenography. Reliance on clinical signs alone may lead to dangerous delay, but roentgenography will show whether the obstruction is persisting.

Sulfathiazole in Pneumococcic Lobar Pneumonia.—Gaisford and Whitelaw employed sulfathiazole in a series of pneumococcic lobar pneumonias and sulfapyridine for alternate patients as controls. Ten patients with true lobar pneumonia were treated with sulfathiazole. There were no deaths and only 1 patient had a complication, an empyema which was drained, with recovery. Among the 9 patients who were treated with sulfapyridine there likewise were no deaths, but 1 patient developed a sterile serous effusion. Sulfathiazole acts similarly to sulfapyridine, but it produces a less prompt fall in temperature. With this temperature lag there is a correspondingly longer period of acute illness. This renders sulfapyridine the drug of choice in severe cases. The chief point in favor of sulfathiazole is that it does not cause vomiting. It is possible that a combination of sulfapyridine and sulfathiazole may come to be a valuable routine in the treatment of pneumonia, the first large doses given being sulfapyridine (e. g. the first 8 tablets) and the following ones sulfathiazole. In this way vomiting can be obviated entirely. An alternative is the use of a mixture of the two drugs from the outset, e. g. 2 tablets of sulfapyridine given with 2 tablets of sulfathiazole fourhourly for the first three doses and then one tablet of each. The first method has already been used since these investigations were undertaken with satisfactory results.

South African Medical Journal, Cape Town

14:331-350 (Sept. 14) 1940

"Eclipse Blindness." J. S. du Toit.—p. 333.
Bilharzial Lesions of Testis. M. Gelfand and G. B. Davis.—p. 334.
Aspects of Civilian Plastic Surgery. J. Penn.—p. 335.
Intramuscular Injection of Uroselectan for Pyelograms in Infants. V. Vermooten.—p. 339.

Chinese Medical Journal, Peiping

58:141-262 (Aug.) 1940

Osteomalacia: Clinical, Metabolic and Pathologic Studies of Case with Parathyroid Hyperplasia and Right-Sided Cardiac Hypertrophy from Thoracic Deformities and Vitamin B_1 Deficiency. S. H. Liu, K. Y. Ch'in, H. I. Chu and H. C. Pai.—p. 141.
Concentration of Sulfanilamide in Aqueous Humor of Human Eyes, with Special Reference to Local Application. T. H. Luo and S. Y. P'an.—p. 167.
Hemolytic Anemia with Erythroblastemia: Report of Three Cases Seen in Chinese Infants. C. Y. Wang and F. Y. Khoo.—p. 177.
Use of Microsedimentation Test in Tuberculous Children. C. Y. Wang.—p. 193.
Study of Aspirated Sternal Bone Marrow in Pellagra. M. S. Hwang, P. T. Kuo and W. Shih.—p. 206.
Inoculation of Monkeys with Leprosy Following Diet of Colocasia: Preliminary Report. D. R. Collier.—p. 213.
Anopheline Mosquitoes of Yunnan; Notes on Their Breeding Habits and Adult Behavior. T. L. Chang.—p. 218.
Some Epidemiologic Observations on Scarlet Fever in Peiping. K. H. Li.—p. 234.
Rat-Bite Fever in Kweiyang: Report of Two Cases. C. S. Yang.—p. 245.

Schweizerische medizinische Wochenschrift, Basel

70:873-900 (Sept. 14) 1940. **Partial Index**

Sulfapyridine and Sulfathiazole in Treatment of Pneumonia. W. Löffler. —p. 873.
*Secondary Effects of Sulfapyridine. R. Hegglin.—p. 881.
*Sulfathiazole Therapy in Epidemic Cerebrospinal Meningitis. W. Pulver. —p. 887.
*Single Massive Doses of Sulfathiazole in Chemotherapy of Gonorrhea. H. Miescher.—p. 891.
Sulfapyridine and Sulfathiazole in Treatment of Furuncles of Upper Lip. F. Wyss-Chodat.—p. 892.
Abdominal War Wounds. T. Naegeli.—p. 894.

Secondary Effects of Sulfapyridine.—Hegglin reports the secondary effects observed in connection with the use of sulfapyridine in more than 450 cases of pneumococcic, meningococcic and gonococcic infections, with granulocytopenia (1 case, terminating fatally) and grave hematuria (5 cases) ranking as the worst effects. Nausea, vomiting, hematoporphyria, mild anemia, cyanosis and cutaneous manifestations (3 per cent) were observed almost regularly. Latent and slowly developing granulocytopenia manifested itself suddenly in a patient with unilateral pneumonia, with high fever, though the drug had been discontinued for some time and the patient felt completely well. Renal lesions were disclosed in grave hematuria, in 1 case evolving into anuria, with increased residual nitrogen. Hematuria often presented a clinical picture of a pronounced renal colic due to calculus, an intense pain extending from one or both kidneys into the testicles and involving only a mechanical lesion, leaving the glomeruli unaffected. Copious water ingestion, regarded by the author as a necessary therapeutic adjuvant in renal stone due to the drug, released large quantities of gravel, acetylsulfapyridine forming the chief constituent. The author believes that, though grave secondary effects cannot be avoided because of the relatively high doses required for treating pneumonic infection, sulfapyridine has proved its chemotherapeutic value. However, the possibility of untoward effects should constantly be borne in mind in order that appropriate counteractive measures may be duly employed. Secondary effects of a nonserious nature, such as nausea and vomiting, may acquire so pronounced an intensity as to necessitate discontinuation of the drug and thus jeopardize the patient's chances of recovery. Granulocytopenia induced by sulfapyridine is not necessarily fatal. An erroneous diagnosis would see in the clinical picture a reactivation of the infection and resume the use of the drug, whereas, in reality, blood analysis would show that damage had been done to the bone marrow. Hematuria ought not to be lightly regarded, as it may lead to anuria. When anuria has set in, cystoscopy is urgently indicated. Sulfapyridine, though parenterally given, was found excreted in the gastric juice, in one case with a 30 per cent concentration. No injurious secondary effects were noted on the nervous system.

Sulfathiazole in Epidemic Cerebrospinal Meningitis.—Pulver found sulfathiazole effective in epidemic cerebrospinal meningitis. Of 26 patients treated solely with this drug (their age level ranged between 1 and 61 years [19 under 16 years]), all recovered save 2, thus yielding a mortality rate of 6.9 per cent compared with a 50 per cent death rate previously noted during a ten year period. Cerebrospinal fluid tests disclosed Neisseria meningitidis in 23 of the cases and its subsequent disappearance within three to seven days after medication. (Nasal and pharyngeal smears had detected the microorganism in only 2 cases.) Blood tests showed in individual cases a decrease in the leukocyte count from 24,800 and 30,200 to 5,800 and 6,700 leukocytes respectively within two days. Biochemical analyses made at regular intervals disclosed a rapid return to normal levels in the sugar, total albumin and chloride content of the blood. The author's experiments in reducing dosage to the lowest quantities compatible with therapeutic effects were finally stabilized at from 12 to 20 Gm. within four to seven days, but allowing for increased dosage in complications. Initial doses in adults of from 1 to 2 Gm. and in children of from 0.1 to 0.15 Gm. per kilogram of body weight and totaling from 6 to 8 Gm. within twenty-four hours were reduced after defervescence to one third and one half of the original dosage. In the majority of cases these quantities of the drug were able to lower fever of 100.4 to 104 F. to subfebrile or normal conditions within twenty-four to forty-eight hours. In order to prevent reactivation the drug was continued for several weeks more. Among the significant effects reported by the author is the observation that some of the children and adults brought to the clinic in a semi or total state of unconsciousness in the morning were able to play in their beds or read the newspaper in the evening. However, headache and cervical rigidity tended to linger for from two to ten days. The drug was administered intramuscularly, in exceptional cases intravenously with dextrose, and caused no local inflammation. Its superior atoxicity was seen in the absence of such secondary effects as granulocytopenia, hemolysis, hepatic lesions, renal irritation and grave cyanosis. A stubborn case of granulocytopenia in a boy aged 8 years with final recovery and a case of neuritis with metastatic acute arthritis of the knee joints are cited by the author as the only evidence of toxic damage produced by the drug. No intraspinal injection was practiced. The drug was found efficacious even in cases of seriously delayed medication.

Sulfathiazole as Chemotherapeutic Agent in Gonorrhea.—Miescher reports the cure of 14 out of 15 male patients, mostly with uncomplicated gonorrhea, by means of a single peroral dose of sulfathiazole. The massive dose, varying between four and ten tablets of the drug (tablet 0.5 Gm.), was either mixed with sugar and placed on the tongue in powdered form or dissolved in water and ingested in 0.5 liter of a native tea. No untoward effects nor relapses were observed. The single dose therapy represents an experimental evolution first from favorable results obtained by combining local and intramuscular vaccines with sulfathiazole for the cure of acute and chronic gonorrhea and then from the exclusive use of sulfathiazole spread over a progressively diminishing period of time. In these experiments the author had observed a reduction in gonococcus count and in gonorrheal discharge usually twenty-four hours, frequently also even twelve hours after medication. Single doses of ten tablets (5 Gm.) are regarded by him as approximating highest levels of tolerance.

Minerva Medica, Turin

2:217-240 (Sept. 1) 1940. **Partial Index**

Eupeptic and Carminative Substances: Clinical Researches for Effects. A. Bellomo and R. Bologna.—p. 217.
*Immediate Action of Liver Extracts on Reticulocytogenic Power of Gastric Juice. G. Lami.—p. 223.

Effect of Liver Extract on Reticulocytogenic Power of Gastric Juice.—Lami studied the reticulocytogenic effect of the gastric juice of 15 normal persons and of 10 patients with pernicious anemia for an hour and a half following intravenous injection of 5 cc. of a liver extract of high potency ("Hepracton"). The gastric juice was removed during fasting and after an injection of histamine alone or preceded one hour earlier by a meal of 100 Gm. of meat. Singer biologic reaction was used to determine the retriculocytogenic power of the gastric juice. The test consists of injecting subcutaneously 3 cc. of neutralized filtrates of the gastric juice to male adult white rats in which the number of reticulocytes is determined before the test. The reticulocyte curve is followed every day for one week. The filtrates can be prepared from the mixture of three or four samples of the gastric juice withdrawn at intervals of fifteen or thirty minutes after the histamine injection following the injection of liver extract alone or preceded by a meal of meat or with the separate samples of the gastric juice. A positive reaction is manifested by an increase in the percentage of the reticulocytes in the blood of the animals and indicates the presence of the antianemic principle in the gastric juice. Failure to change on the part of the reticulocytic curve indicates a negative reaction and absence of the antianemic principle in the juice. The highest figures in the reticulocyte curve occur on the second, third or fourth day of the test, which gives a positive result in normal persons and in achylic hypochromic anemia and negative results in pernicious anemia. The positive results agree with those of the Castle test. In the cases observed by the author the reticulocytogenic power of the gastric juice of normal persons was increased after the injection of the liver extract (strong positive results of the Singer test). The increase was greater when the test included a meal of meat than when it did not. The reticulocytogenic power of the gastric juice of

patients with pernicious anemia in remission from liver therapy was greatly diminished before administration of the liver extract (weak positive results of the Singer test) and did not change after administration of the extract. The gastric juice of patients with pernicious anemia who had not had liver therapy did not possess reticulogenic power before administration of the liver extract (negative results of the Singer test) but increased after administration of the extract. The author believes that liver extract injected intravenously stimulates the absorptive capacity of the gastric wall and upper segment of the intestine for the antianemic principle and stimulates the production of the endogenic factor which results in a better use of the exogenic factor and consequent production of the antianemic factor. The latter, as soon as it is stored in the liver, stimulates the gastric wall and the upper segment of the intestine to further production of exogenic factor and to hemopoiesis. Liver extract injected intravenously acts through a mechanism of stimulation. It acts as substitution therapy only when the gastric wall and intestine are the seat of grave pathologic lesions.

Monatschr. für Ohrenheilkunde, Berlin

74:99-152 (March) 1940

Otorhinolaryngologic Literature of Scandinavian Authors for the Year 1938. E. Jerlang.—p. 99.
*Vitamin Therapy in Otosclerosis. M. Baer.—p. 113.
Speech—Psychologic Observations. K. Baldrain.—p. 118.
Cutaneous Horn of Right Auricle: Case. H. Schnaubelt.—p. 125.
New Instrument for Maxillary Sinus Puncture. S. Krepuska.—p. 128.

Vitamin Therapy in Otosclerosis.—Baer reports unsuccessful results in experiments undertaken to modify otosclerosis in 15 cases by means of vitamins C and B_1 and a regimen rich in these vitamins, employed for several months at a time. Subjective symptoms such as headache, vertigo, anorexia and tinnitus aurium were favorably affected and the improvement credited to vitamin B_1. The author encountered a vitamin C impairment of from 600 to 1,500 and even 2,000 mg. but does not believe in a direct connection between general vitamin C deficiency and otosclerosis. Irrespective of the vitamin C index, he fed vitamins in concentrated doses to all otosclerotic patients on the assumption that a local vitamin deficiency may well coexist with a systemic sufficiency, as is seen in paradentosis, in which the osseous changes resemble those of otosclerosis and even permanent cures seem to be effected by vitamin C. He inclines to the view that otosclerosis represents a new bone growth and hence an osteitis fibrosa, which may be hereditary in some cases. The general ineffectiveness of therapeutic measures to influence otosclerosis justifies any rational experimentation. Besides, vitamins ineffective in relation to the otosclerotic process may increase the efficacy of other medicaments employed to influence the pathologic process.

Acta Ophthalmologica, Copenhagen

18: 1-107 (No. 1) 1940

*Malignant Exophthalmos After Strumectomy. V. A. Jensen.—p. 1.
Demonstration of Absorption Curve of Dyestuff in Macula of Dead Macacus. E. Hanström.—p. 21.
Nodulate Iritis (Iritis Boeck?): Three Cases. P. Kindt.—p. 38.
Anisochromatopsia Congenita. G. W. Keyser.—p. 51.
Rare Deformity of Upper Tear Passages in Young Girl. G. W. Keyser.—p. 55.
A Family with Groenouw's Keratitis. H. Malling.—p. 58.
Conjunctival Lymphoma. J. P. Jensen.—p. 67.
Scleredema with Ophthalmologic Changes: Case. A. Stenbeck.—p. 76.

Malignant Exophthalmos After Strumectomy.—Jensen describes four cases of exophthalmic goiter in which malignant exophthalmos developed after strumectomy. Malignant exophthalmos is characterized by a rapid and violent progression. In the beginning the patients complain only of conjunctival discomfort due to smarting pain, injection and profuse epiphora. These symptoms become manifest several months after a successful strumectomy which led to the disappearance of all hyperthyroid symptoms with the exception of ocular proptosis. Then there appear peculiar pasty thickenings of the eyelids and of the integument surrounding the eyes and pronounced chemosis with coincident aggravation of the bulbar protrusion. Violent headache develops and a painful sensation of tension across the eyes. The protrusion of the eyeballs becomes so excessive that they are almost immobile. Enormously chemotic conjunctivas bulge out like shining red projections between the eyeballs and eyelids. Vision may become impaired as the result either of changes in the optic nerve or of the lagophthalmic keratitis, which attacks the unprotected cornea. In favorable cases in which the proptosis stops spontaneously or is checked by operation the corneal infiltrations heal, leaving leukomas, but usually they change into necrosis with perforating ulcerations and panophthalmia necessitati. g bilateral exenteration of the eyeballs. After removal of the eyeball the swollen orbital contents may prolapse for months through the palpebral slit, but then they undergo a gradual diminution. Malignant exophthalmos is comparatively rare. The literature contains reports of about eighty cases. Compared with the enormous number of strumectomies the rareness of malignant exophthalmos suggests that special conditions not directly concerned with the operation or the decrease of thyroid hormone make the appearance of the protrusion possible. Hyperthyroidism and proptosis may be coordinated, mutually independent phenomena. The question arises whether their common cause might be a secretory disturbance in the anterior lobe of the pituitary. This theory is supported in two different ways: (1) The adenohypophysis has a regulating influence on the function of the thyroid and (2) certain hypophysial disorders, such as Cushing's disease and acromegaly, may be attended by protrusion of the eyeballs. Experimental research suggests that malignant exophthalmos might be caused by hyperactivity of the anterior lobe of the hypophysis concurrent with a postoperative reduction in the function of the thyroid. In the beginning, corneal desiccation may be prevented by tarsorrhaphy, conjunctival plastics or bandaging with petrolatum and gutta-percha paper, but it will soon become necessary to try canthotomy and relaxing incisions in the chemotic conjunctiva and along the base of the eyelids, eventually combined with removal of orbital fat. Roentgenization of the orbit seems to be without effect. Since proptosis necessitated bilateral exenteration in many cases of malignant exophthalmos, more extensive operations have been taken into consideration. Dollinger's procedure of cutting a wedge-shaped piece of bone out of the lateral orbital wall, although successful in excessive ophthalmic goiter, has as yet not been tried in malignant exophthalmos. Naffziger suggested intracranial decompression of orbit and optic canal. With Naffziger's technic access is obtained transfrontally by two flaps of bone to the anterior cranial fossa, where the orbital roof and the upper wall of the optic canal are resected, after which the orbital fascia is opened and a relaxing incision is made in the annulus zinnii. Naffziger later extended the operation by removing also the temporal and a little of the posterior wall of the orbit. Immediately after the operation the protrusion is seen to decrease, the eyes become more mobile, the corneal ulcerations heal and the visual acuity improves. A third method suggested by Sewall and successfully applied by Kistner is the radical removal both of the frontal sinus and of the ethmoid cells. Sewall's operation supposedly is easier than Naffziger's and the resulting cicatrices are smaller. Naffziger's or Sewall's operation should be carried out as soon as the first signs of incipient optic neuritis or of corneal ulceration are observed.

Nordisk Medicin, Gothenburg

7: 1337-1372 (Aug. 10) 1940. **Partial Index**

Hospitalstidende

*Essential Juvenile Anemia Due to Iron Deficiency (Chlorosis). G. Alsted.—p. 1338.
Two Cases of Cushing's Syndrome in Men. E. W. Flensborg.—p. 1342.

Essential Juvenile Anemia Due to Iron Deficiency (Chlorosis).—Alsted describes the six cases observed in the medical department of the Frederiksberg Hospital during the last ten years. The age distribution is somewhat higher than that reported in earlier cases and menstrual disturbances seem less frequent. There were indications that the diet had been quantitatively and qualitatively deficient. The patients responded well to massive iron therapy, a rise of 1,000,000 erythrocytes occurring within a week. The author proposes the term "essential juvenile iron deficiency anemia" instead of chlorosis.

THE STUDENT SECTION

of the

Journal of the American Medical Association

Devoted to the Educational Interests and Welfare of Medical Students, Interns and Residents in Hospitals

SATURDAY, DECEMBER 21, 1940

Opportunities in the Practice of Medicine

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Medicine probably is the only field today in which a well educated graduate is sure of making a living and also of having security if he carries disability, life and old age insurance. Except for crowding in the larger cities, there is no unemployment problem for American medical graduates. Although he will not make a fortune, as large medical incomes may be a thing of the past, the average physician's income at present probably is at its highest level. According to national figures, 30 per cent of the three and one half billion annual total cost of medical care is for physicians, or $3,800 net per physician. However, this net figure is based on many physicians who are not in practice, and the correct average net income probably is higher. "Average incomes" may be misleading. A few very large incomes do not help the physician who is not earning enough to enable him to maintain the standards of good practice. However, physicians with extremely high and low incomes are in the minority; no physician's income can be compared with those of the leading lawyers, but physicians have not found it necessary to seek other fields to eke out an existence, as is the case with some lawyers.

One of the reasons for this difference in the status of physicians and lawyers is that the ratio of the former to the population has been declining during the past century from 1:569 (including all healers) in 1850 to 1:742 in 1940.[1] Though medical students have increased during the last twenty-five years from 14,891 to 21,302 in spite of the reduction of the medical schools from ninety-six to seventy-seven, the population has expanded faster than the medical graduates.[1] Raising the educational standards of modern physicians, the improved quality of present medical service and the increased recognition by the public of the need for better medical care also are factors in the present status of the medical profession.

The standard of a physician's living depends on his medical training, professional and business ability, energy, personality, common sense, location, hospital and other affiliations and his specialty, including general practice as a specialty. The first six of these factors are obvious, but the last three need discussion.

LOCATION

Other areas also may need medical service, but in the South the ratio of physicians to the population is 69 per cent lower than in the North (table 1). That this dearth is not primarily due to the reduction of American physicians but rather to their maldistribution is indicated by the fact that during the last thirty years the concentration of medical men in the Northern urban states decreased only 3 per cent, from a ratio of 1:609 in 1906 to 1:629 in 1936, which is still too high, while in the South the reduction was 21 per cent to 1:1,063. In some Southern counties the ratio of physicians to population is as low as 1:4,500,[2] although 1:1,000 is considered necessary, especially in rural communities.[3] Conclusions that the medical profession is overcrowded and that the condition can be relieved by reducing the number of students entering our medical schools,[4] though correct for New York, Boston, Philadelphia and Chicago, are invalid for the South or any other predominantly rural area. Over half of the 241 counties in the United States with inadequate medical service are in the ten Southern states.[5] The distribution of medical services, physicians, hospitals and nurses is more impor-

Read at the dedication of the new hospital buildings of the Lynchburg General Hospital, Lynchburg, Va., May 21, 1940.

From the Department of Pediatrics, Duke University School of Medicine and Duke Hospital, with the assistance of Miss Judith Farrar, Librarian of Duke Hospital. Many of the data were abstracted from Davison, W. C.: A Survey of Medical Education in the South, address at the inauguration of Oliver C. Carmichael as Chancellor of Vanderbilt University, and a Symposium on Higher Education in the South, Nashville, Tenn., Vanderbilt University, Feb. 4, 1938.

1. Cutter, W. D., Secretary, Council on Medical Education and Hospitals: Personal communication to the author.

2. Duke Endowment, Hospital Section, Third Annual Report, 1927.

3. Final Report of the Commission on Medical Education, New York, Office of the Director of Study, 1932.

4. Bevan, A. D.: The Overcrowding of the Medical Profession, J. A. Am. M. Coll. 11:377-384 (Nov.) 1936. Final Report of the Commission on Medical Education.[3]

5. Rural Medical Service, Chicago, American Medical Association, Bureau of Medical Economics, 1937.

tant than their actual number. There is more hazard to the public and to the medical profession from scarcity of physicians in certain areas than from overcrowding in others.[6]

This uneven distribution is even worse if it is remembered that the average age of physicians

TABLE 1.—*Population per Physician in 1936*

State	Population (1934)	Physicians (1936)	Population per Physician
Ten Southern States			
Alabama	2,710,000	2,105	1,287
Florida	1,575,000	1,939	812
Georgia	2,911,000	2,765	1,052
Kentucky	2,657,000	2,770	959
Louisiana	2,166,000	2,135	1,014
Mississippi	2,057,000	1,515	1,358
North Carolina	3,301,000	2,570	1,284
South Carolina	1,750,000	1,335	1,311
Tennessee	2,676,000	2,939	911
Virginia	2,446,000	2,734	895
Subtotal	24,249,000	22,807	1,063
Four Northern Urban States			
Illinois	7,876,000	11,672	675
Massachusetts	4,335,000	7,263	597
New York	13,059,000	24,013	544
Pennsylvania	9,826,000	12,889	763
Subtotal	35,096,000	55,837	629
(Total U. S. A.)	118,724,606	165,163	719

in rural counties is 52 years.[7] In Tennessee, for example, only 43 per cent of the physicians in the cities are over 50 years of age, in contrast to 77 per cent of those in the rural areas.[6]

Another disturbing condition in the rural areas is the paucity of recent graduates; 51 per cent of the young graduates located in places under 5,000 population in 1906, but only 11 per cent of the graduates of 1915 and merely 9 per cent of the class of 1920,[8] although 48 per cent of the population live in communities under 5,000.

FACTORS RESPONSIBLE FOR SCARCITY OF PHYSICIANS IN RURAL AREAS

The three factors apparently responsible for the scarcity of physicians in the South or in any other rural area are the financial return, scattered population and living conditions.

Financial Return.—A survey[9] of three rural counties in Tennessee, Georgia and Mississippi in 1931 demonstrated that the money spent for medical care was inadequate to remunerate practitioners or to support hospitals and other medical facilities. Three reasons tend to be responsible for this low economic status: (1) The per capita spendable money is low, (2) a year of unfavorable weather or a lowered market for cotton, the chief "money" crop, creates a depression and (3) the Negro population decreases the economic average and increases the need for medical care. However, voluntary hospital care associations will greatly improve the situation. For example, the annual hospital bills in these three counties varied from nothing to $319, but if spread over the population the annual cost would have been 98 cents per capita. If hospital bills can be met, the people usually can and do pay their professional charges. A recent survey of the capacity of the various states to absorb more physicians, based on their need for and ability to support medical service (table 2), ranked the ten Southern states eighteenth to thirty-ninth.

At present, owing to the improvement in farming conditions but more especially to the dearth of physicians and to the absence of competition, the incomes of the keener rural doctors often are equal to those of their urban brethren, and even better if the cost of living is considered. In some areas, subsidy by the community has been attempted, although this policy generally has been unsatisfactory.[10] In recent years, the number of rural physicians increased 8 per cent without subsidies.

Scattered Population.—Although the density of the population is increasing in the Southern states, the rate has not been as rapid as in the North (table 3). Obviously the maintenance of a practice and of a hospital is more difficult in an area with fifty-three people per square mile than in one with 286. Furthermore, the distribution of physicians in the Southern states naturally follows the density of the population. The area per physician in North Carolina in 1927 ranged from 3.6 square miles in an urban

TABLE 2.—*Relative Capacity of the Southern States to Absorb More Physicians* *

Based on Their Need for and Ability to Support Medical Service

State	Rank Among the 48 States and District of Columbia	State	Rank Among the 48 States and District of Columbia
South Carolina	18	Mississippi	28
Florida	19	Virginia	30
North Carolina	21	Kentucky	36
Alabama	22	Tennessee	38
Georgia	24	Louisiana	39

* Harris, D.: Opportunities for Medical Practice in the United States, Medical Economics **17**: 42-47 (June) 1940.

county to 203.8 square miles in a rural area, with an average of 21.7 square miles per physician.[2] Improved roads, however, have greatly reduced the time consumed in making visits.

Living Conditions.—Rural life is all right if one likes it, but only those of us who were

6. Hyman, O. W.: Southern Medical Colleges Must Maintain Enrolment at Least at Its Present Level, J. A. Am. M. Coll. **12**: 301-304 (Sept.) 1937; The Number and Distribution of Physicians in the Southern States as Bearing on the Policies of Southern Medical Colleges, South. M. J. **30**: 85-89 (Jan.) 1937.

7. Pusey, W. A.: The Trend in Medical and Nursing Services, J. A. M. A. **82**: 1960-1964 (June 14) 1924; Medical Education and Medical Service: Further Facts and Considerations, J. A. M. A. **86**: 1501-1508 (May 15) 1926.

8. Duke Endowment, Hospital Section, First Annual Report, 1925. Mayers, L., and Harrison, L. V.: The Distribution of Physicians in the United States, New York, General Education Board, 1924. Rappelye, W. C.: Discussion, Bull. A. Am. M. Coll. **2**: 46 (Jan.) 1927. Weiskotten, H. G.: Present Tendencies in Medical Practice, ibid. **2**: 29-47 (Jan.) 1927; Tendencies in Medical Practice: A Study of 1925 Graduates, J. A. Am. M. Coll. **7**: 65-85 (March) 1932.

9. Guild, C. St. C., and Falk, I. S.: Surveys of the Medical Facilities in Three Representative Southern Counties, Publication 23, Committee on the Costs of Medical Care, Chicago, University of Chicago Press, 1932.

10. Pusey, W. A.: Medical Education and Medical Service, J. A. M. A. **84**: 281-285 (Jan. 24), 365-369 (Jan. 31), 437-441 (Feb. 7), 513-515 (Feb. 14), 592-595 (Feb. 25) 1925. Ordway, Thomas: A Medical School's Effort to Provide Physicians for Rural Communities, Proc. Ann. Cong. Med. Educ., 1929, pp. 28-30.

raised in the country appreciate its charm, even though the radio, movies and better roads are rapidly ameliorating the isolation and lack of amusements and are improving the living conditions. However, the social factor of unfamiliar surroundings, as well as the uncertainty of financial returns, probably deters the surplus city physicians from migrating into the country.[6] Not only are "city raised" physicians unhappy if they locate in the country but their patients often do not like them. A few "city raised" physicians have settled from time to time in one rural county with one physician to 4,000 of the population but moved away within a year as they could not establish practices, although the "country raised" physicians in that area have more than they can do and welcomed additional practitioners.

TABLE 3.—*Density of Population per Square Mile* *

State	1910	1930
Ten Southern States		
Alabama	41.7	51.6
Florida	13.7	26.8
Georgia	44.4	49.5
Kentucky	57.0	65.1
Louisiana	36.5	46.3
Mississippi	38.8	43.4
North Carolina	45.3	65.0
South Carolina	49.7	57.0
Tennessee	52.4	62.8
Virginia	51.2	60.2
Average	43.07	52.77
Four Urban Northern States		
Illinois	100.6	136.2
Massachusetts	418.8	528.6
New York	191.2	264.2
Pennsylvania	171.0	214.8
Average	220.40	285.95

* U. S. Bureau of Foreign and Domestic Commerce: Statistical Abstract of the United States 58, Washington, D. C., Government Printing Office, 1936.

The South will not get its physicians by migration; the students should be Southern, and to get country doctors it must be possible for students from the rural counties to study medicine. "We are oblivious to social facts in trying to devise some plan to get our graduates to go to the country. That is impossible with city graduates. Our real problem is to devise a plan whereby we can get students to come from the country. They are the ones from whom the rural practitioner must be recruited. The country lawyer, the country preacher, the country banker and business man, as the country doctor, do not go from the cities; they come from the country. And unless we succeed in devising some exotic substitute which the country will accept, we shall have to devise some plan whereby the country doctor can be developed from the country boy."[7] Graduates tend to return to the environment to which they are accustomed. For example, 83 per cent of the country students at the University of Tennessee returned to rural practice, and 80 per cent of the urban youths later practiced in the city. In Tennessee a campaign of publicity from 1925 to 1930 called attention to the need for country doctors. The ratio of students from rural counties at the University of Tennessee College of Medicine responded at once, and by 1927 the number of graduates going into country practice began to increase.[6] No accurate figures are obtainable on the percentage of rural students in other medical schools compared to the ratio thirty years ago, but apparently it is much lower.

Rural students, owing to the poverty of farmers, rarely are wealthy or have resources for raising money. Probably the best way by which a sufficient number of country students can attend medical school is through loan funds, which can be repaid over a period of years and thus become available for future students. Scholarships, such as those of the Commonwealth Fund, for students who agree to practice in the country, are splendid and have demonstrated their success but require too great an outlay to be widely available and usually do not create in graduates a healthy sense of obligation toward their community and university. A revolving loan fund on which 6 per cent interest is charged is an ideal investment for university endowment funds, as medical students can and do repay their debts, and it will enable keen rural students to return to country practice. Medical schools should trust their product; if they have no confidence in them, who will? Duke students after their first year may borrow up to $450 a year at 6 per cent,

TABLE 4.—*Population per Hospital Bed in 1936*

State	No. of Approved Hospitals *	Total Approved Hospital Beds	Population per Bed
Ten Southern States			
Alabama	4	1,296	2,091
Florida	3	745	2,114
Georgia	7	1,606	1,813
Kentucky	8	1,762	1,508
Louisiana	8	3,934	551
Mississippi	0	0	0
North Carolina	11	1,797	1,837
South Carolina	4	1,109	1,578
Tennessee	10	2,679	999
Virginia	7	1,542	1,586
Total	62	16,470	1,472
Four Northern Urban States			
Illinois	54	12,787	225
Massachusetts	35	9,888	438
New York	96	37,959	344
Pennsylvania	78	23,156	424
Total	263	83,790	419

* These hospitals have 50 per cent of the total bed capacity of the United States, although they represent only 10 per cent of the total number of hospitals.

and the principal is repaid in instalments starting two years after graduation. An average of $10,000 lent annually has enabled practically every Duke medical student to continue his education. A state which needs physicians could obtain them, not only without cost, but actually at a profit by establishing similar loan funds. Cheaper medical education is not a solution.

HOSPITAL FACILITIES

The distribution of physicians and that of hospitals are mutually dependent. Physicians rarely will practice and remain in a community without hospitals, and a hospital without adequate medical personnel is not a hospital but a somewhat dangerous hotel. The young, highly trained physician of today does not feel that he can practice modern medicine without access to a hospital. Even though 90 per cent of patients can be and are properly cared for in their homes or in the physician's office,[11] the laboratory facilities of a hospital are essential for the diagnosis of many conditions. The establishment and maintenance of rural hospitals in North and South Carolina with the aid of the Duke Endowment not only is improving the medical service in the country but also is attracting young graduates there. In addition, local hospitals influence the older physicians who have kept abreast of the times to remain in rural communities. One of the major objectives of the Duke Endowment is to bring about a better distribution of well trained physicians by an improvement and an extension of available facilities for the practice of modern medicine which exist in and not apart from hospitals.[12]

A complete medical service is a tripod of which the three legs are (1) hospital facilities, (2) nurses and technicians and (3) physicians,[13] the last being the basic element. Modern medicine often is unsatisfactory without modern facilities not only for the seriously sick who are brought to the hospital but also for the less seriously ill who are to be found in their homes throughout the country. The influence of the location of hospitals on the distribution of physicians is strikingly illustrated in North Carolina; in the fifty-seven counties which have hospitals there is one physician to every 1,149 people, and in the forty-three counties without hospitals the ratio is 1 to 2,034.[14] Of the 638 ten year graduates who have settled in North Carolina since 1925, only sixty-four located in towns without hospitals.[15]

The phenomenal growth of hospitals in the United States has been reflected in the South, but the Southern hospitals still have a much smaller average number of beds, and the population per hospital bed is thrice that of the urban North (table 4).

Not only do rural communities need hospitals, but equally important, if they have a hospital, they require financial assistance to enable the people to use the hospital. Bed occupancy is as vital as the beds themselves. Modern medical service cannot exist without hospitals, and hospitals cannot survive without support from endowments, state, county or federal aid, or voluntary hospital care associations. Because of present financial conditions, endowments are becoming rare, and state, county and federal aid may bring political control.[16] The voluntary group hospital care association seems to be the logical answer. England started the movement, and Texas and North Carolina demonstrated its practicability in the South. Church gifts to hospitals help, but the hospital contributions of the 2¾ million members of one denomination have averaged less than 1.5 cents per member annually, while the Hospital Care Association in Durham, N. C., paid the hospitals an average of $7.13 per member annually.

SPECIALTY

The answer to the question "Is the general practitioner doomed?" is "No," and that to the query "Is the profession overspecialized?" is "Yes." It is true that only 25 per cent of the recent graduates intend to do general practice,[8] that the number of general practitioners has been steadily growing less, and that the average age of those left is increasing. However, as a well trained general practitioner can and does successfully treat over 80 per cent of disease, and as his volume enables him to treat his patients at a lower cost, the public needs and wants more general practitioners. The fact that 75 per cent of the present graduates are or plan to be specialists who are needed by less than 20 per cent of the patients is an indication not only of the overcrowding of the specialties but also of the urgent need and wide open opportunities for good general practitioners. This plethora of specialists has caused such competition and crowding that in many Southern communities the financial rewards of general practitioners, with their reduced competition, are higher than those of specialists. The modern medical curriculum often is blamed for this trend toward specialization, but the tide toward general practice is turning without any changes in the medical schools; it is a response to economic conditions.[17] Since the law of supply and demand is causing a larger percentage of the present graduates to enter general practice, it behooves medical schools to study this field so that students may be better prepared for it.

An analysis of the diseases treated by Tulane graduates indicates that a general practitioner's visits consist of obstetrics and gynecology 10 per cent, minor surgery 15 per cent, and the remaining 75 per cent divided among sixty-eight common conditions. Ninety per cent of

11. Council on Medical Education and Hospitals, Report, J. A. M. A. **80**: 1928-1937 (June 30) 1923.
12. Duke Endowment, Hospital Section, Fourth Annual Report, 1928; Tenth Annual Report, 1934. Rankin.[38]
13. Rankin, W. S.: Hospitalization, South. M. J. **24**: 1113-1115 (Dec.) 1931.
14. Rankin, W. S.: The Interest of the Hospital Section of the Duke Endowment in Medical Education, Proc.Ann.Cong.Med.Educ., 1929, pp. 38-40.
15. Duke Endowment, Hospital Section, Tenth Annual Report, 1934.
16. Does Federal Subsidy Mean Federal Control? editorial, J. A. M. A. **110**: 132 (Jan. 8) 1938.
17. Davison, W. C.: Duke University School of Medicine, Tr. M. Soc., N. C. **74**: 35-39, 1927.

general practice is done outside the hospital, approximately 55 per cent in the office and 35 per cent in the home. About 75 per cent of office visits are for minor surgery, respiratory infections, general medical disorders and venereal diseases, and 90 per cent of home visits are for respiratory, general medical and contagious diseases, obstetrics and minor surgery.[18]

A generation ago general practitioners spent most of their time treating children. Now, with the ratio of children to the total population reduced during the past twenty years from 1:3 to 1:4, with diphtheria, whooping cough, dysentery and typhoid becoming rarities, with pneumonia and meningitis successfully treated with sulfapyridine or other drugs, with congenital syphilis reduced through the expansion of the program for treating pregnant women, with infant feeding simplified, and with the mortality in children decreased 66 per cent, most of a general practitioner's present patients are adults.[19] However, the need for preventive pediatrics cannot be overemphasized; 75 per cent of the deaths among children are preventable. The distribution of a general practitioner's income also has changed. Formerly approximately 50 per cent came from obstetrics, in contrast to 30 per cent of his time,[20] 25 per cent from pediatrics, in contrast to 50 per cent of his time, and 25 from adult medicine, in contrast to 20 per cent of his time. A recent analysis reported 20 per cent of a general practitioner's income from obstetrics, 30 per cent from pediatrics and 50 per cent from adult medicine.[21] The percentages of time spent in each group were similar to those of the income.

One difficulty in persuading young graduates to go into general practice is their erroneous feeling that it does not carry the same dignity as that of a specialty. Since the specialty boards were created, the students have increasingly obtained the impression that general practice is what the specialists discarded. As a matter of fact, general practice is just as much a specialty as pediatrics, and the present misunderstanding would be corrected if general practice had its own specialty board and requirements. The general practitioner needs a sound scientific background as much as if not more than a specialist, so that he may be capable under all circumstances of advising the family whether the patient needs to consult a specialist.[22] A rural physician needs a more prolonged training than a city practitioner, for he must be better able to meet his problems unaided.

18. Bass, C. C.: Relative Proportion of Diseases and Conditions Treated by Our Graduates in Their Practice, South. M. J. **21**: 1049-1054 (Dec.) 1928. Rappelye, W. C.: Discussion, South. M. J. **21**: 1053 (Dec.) 1928.
19. Time **35**: 49 (May 13) 1940.
20. Rowland, J. M. H.: Clinical Teaching of Obstetrics, Proc. Cong. Med. Educ., 1930; also Tr. A. Am. M. Coll.
21. Hamner, J. L., and Lackey, W. J.: A Month of General Practice, South. Med. & Surg. **101**: 625 (Dec.) 1939.
22. Welch, W. H.: Changing Viewpoints in Medical Education, South. M. J. **24**: 1121-1124 (Dec.) 1931.

All graduates, and especially those desiring to enter general practice, should spend at least two years in hospital work. This is required of Duke graduates, and 80 per cent of them have spent more than this minimum. These internships preferably should be "straight" services rather than "rotating," which often provide merely a smattering of several subjects. If a graduate plans to enter general practice—a consummation much to be desired—a straight medical internship for one year, a straight pediatric internship for six months and a straight obstetric internship for six months would equip him much better than the usual rotating service. Duke Hospital has made this training possible by adding to its "straight" internships in other fields a combined obstetric-pediatric internship of one year. Three months of this time is spent in hospital obstetrics and gynecology at Duke under Dr. Bayard Carter, three months on the Outside Obstetrics Service, Charlotte, N. C., under Dr. W. Z. Bradford, five months in hospital pediatrics at Duke and one month on infectious diseases at the Sydenham Hospital, Baltimore, under Dr. M. G. Tull. It is hoped that all state boards of licensure will recognize straight internships in any field rather than only rotating services.

TABLE 5.—*Graduates of the Southern Schools of Medicine in 1936*

Medical Schools in the Ten Southern States	Number of 1936 Graduates
Alabama	0*
Georgia	33
Emory (Georgia)	55
Louisville (Kentucky)	89
Louisiana State University	43
Tulane (Louisiana)	113
Mississippi	0*
Duke (North Carolina)	54†
South Carolina	45
Tennessee	102
Vanderbilt (Tennessee)	51
Meharry (Tennessee)	35
Virginia, University of	61
Virginia, Medical College of	82
Total	763

* The students of the two year schools are not included, as some of them subsequently are graduated from other Southern schools, although many go to Northern schools.
† University of North Carolina and Wake Forest College also have two year schools, and the latter is starting a four year curriculum in 1941.

SUMMARY

Even though certain factors have decreased the demand for medical personnel, e. g. the reduction of preventable diseases and the increase in telephones, hospitals and nursing, the South, in order to have adequate medical service, needs nearly twice the present number of physicians (table 1) and a threefold increase in hospital beds (table 4), especially in the rural areas. The problem is to find the former, build the latter and support both of them. The twelve Southern four year schools graduated 763 physicians in 1936 (from thirty-three to

113 per school; table 5). If all of them settled in the South, and they do not, they barely would replace the losses by death among the 22,807 physicians in the ten Southern states.

The solution is threefold: improving Southern medical schools, expanding Southern hospitals and making possible the education of Southern country youths. The first is being done rapidly by the cooperative efforts of the universities and the foundations, the second can be accomplished by voluntary hospital care associations, and the third requires the establishment of loan funds for students from rural areas so that more Southern students can obtain a medical education and become Southern rural general practitioners.

Studying Tropical Medicine in Puerto Rico

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Last February a notice appeared on the bulletin board at Long Island College of Medicine about an opportunity for third year students to study tropical medicine in Puerto Rico. We applied and learned of the teaching project instituted by Dr. Thomas J. Le Blanc, professor of preventive medicine at the University of Cincinnati College of Medicine, and Dr. George W. Bachman, director of the School of Tropical Medicine in San Juan, Puerto Rico. Under this plan, small groups of students had, in two previous years, spent part of the summer between the third and fourth years in San Juan engaged in brief but intensive study of tropical medicine in its natural setting. Staff members of the school and of the insular health department and various hospitals and clinics in San Juan and elsewhere cooperated in the teaching program.

We sailed, June 13, on the S. S. *Coamo*. The passengers were mostly university and preparatory students returning to their homes in Puerto Rico for the summer. We were impressed with their charm, vivacity and torrents of musical language, which were too much for our Spanish. We made many acquaintances among Puerto Rican students of dentistry, parasitology, bacteriology and medicine.

The School of Tropical Medicine is one of the outstanding architectural achievements in San Juan, patterned after the Palacio de Monterey in Salamanca, Spain. The school program consisted of one week each of study in entomology, pathology, mycology and public health and two weeks of clinical work. The first week was spent under the guidance of Dr. William Hoffman, medical zoologist, who had been in Puerto Rico fourteen years. We studied the taxonomy of mosquitoes and observed in the laboratory the eggs, larvae and adults of various species of Anopheles, Culex and Aedes. Then we went into the field, visiting heavily infested areas and collecing larvae and adult forms. We had the experience, quite discouraging for the novice, of dissecting mosquitoes under the microscope looking for filariae.

In the parasitology laboratory was an amazing collection of material for the study of parasites prevalent in Puerto Rico and elsewhere. The laboratory studies were supplemented by excursions to the haunts of the insect vectors, in the course of which we absorbed information concerning the local flora, fauna and mores.

The last day in the department of medical zoology was devoted to field work on a larger scale. We observed poorly protected cesspools and other breeding places for mosquitoes in the vicinity of human habitations and found the larvae of Anopheles in abundance. We searched for the molluscan host of Schistosoma mansoni, the fresh water snail Australorbis glabratus, which thrives in the contaminated waters of certain streams. As we collected snails, small boys wading in the streams were seen to have splenomegaly and ascites characteristic of schistosomiasis. This was a forceful demonstration of the presence of this disease in these river valleys.

The week end was spent traveling across the island visiting hospitals, clinics and other places. We left San Juan and drove along the old Spanish road, the Carretera Militar, through Rio Piedras, Caguas, Cayey, Aibonito, Coamo and Juana Diaz, reaching Ponce on the Caribbean coast. In Ponce we visited La Clinica Pila, Tricoche City Hospital and St. Luke's Hospital, where much clinical material was demonstrated to us. From St. Luke's, which is on a hill, could be seen the entire city and in the distance the aptly named island Caja de Muerto, which rests on the Caribbean Sea like a giant coffin. The next stop was the Ryder Memorial Hospital in Humacao, where some unusual cases of tropical disease were demonstrated.

At Santiago Island we visited what is said to be the world's only free range primate colony. Afterward we drove through the Caribbean National Forest, up to the crest of El Yunque, where the vegetation was of rare variety and interest.

The second week at the School of Tropical Medicine was devoted to the pathology of tropical disease and the special problems connected with the practice of medicine in the tropics.

Under the teaching of Dr. Enrique Koppisch, these studies were carried out in a large room in the tower, which commanded a view of the harbor, the airport, the mountains, the city and the ocean. This week was given to malaria and blackwater fever, schistosomiasis, chromoblastomycosis, the filarial diseases, elephantiasis, leprosy, madura foot and mossy foot, sprue, balantidiasis, yellow fever, yaws, ainhum and hydatid disease. The reading of necropsy protocols and references to the literature supplemented microscopic studies of diseased tissue. Dr. Koppisch presented the material with such clarity that this week proved to be the backbone of our studies in Puerto Rico.

In the study of hematology Dr. Rodriquez-Molina emphasized the anemia of sprue, which is common in Puerto Rico. The secondary anemias associated with uncinariasis, the blood changes in malaria and in schistosomiasis, and the high incidence of eosinophilia in Puerto Rico were discussed. Almost a week was spent in studying mycology. The climate of Puerto Rico is conducive to the growth of fungi. Lectures were supplemented by the study of cultures and by clinical contacts with the diseases discussed.

A week with the Department of Health impressed us with the work being carried on under the dynamic Commissioner of Health, Dr. Garrido Morales. We saw the subsoil drainage program of malaria control, from the making of the cement pipes to their installation with subsequent conversion of malarial swampland into cane fields. Hookworm is being controlled by the distribution of latrines manufactured by mass production methods. Tuberculosis, a serious problem in Puerto Rico, is vigorously attacked. We visited the sanatorium at Rio Piedras, the clinics devoted to the pneumothorax treatment of ambulatory patients, venereal clinics, bacteriologic laboratories, pediatric clinics, health centers in the smaller towns, the mental hospital and the leper colony, where there were fifty-four lepers.

The clinical work consisted of ward rounds at the University Hospital of the School of Tropical Medicine, the Presbyterian Hospital and the Bayamon District Hospital, the latter the first of a number of projected 300 bed well equipped district hospitals. The ward rounds brought us to realize that, although tropical diseases may present themselves as single diagnostic entities, they more often appear in conjunction with other diseases which constitute the problems of general medicine.

We returned to El Yunque for a farewell party with those who had so hospitably received us. On August 5 we were back in New York.

Digests and Reviews

MEDICAL EDUCATION

Abstract of remarks by A. Lawrence Lowell, President of Harvard University, Boston, published in the New England Journal of Medicine, March 21, 1940.

Education in medicine is more difficult than that in any other profession because it involves the knowledge of many subjects which, apart from their relation to medicine, have no natural connection. In a medical curriculum, gross anatomy has to the beginner no obvious connection with biologic chemistry, bacteriology or pharmacology. Each involves a brute effort of memory and is largely forgotten before the time comes for its application to the practice of medicine or surgery. Whether there is an advantage in learning more facts than can be retained depends on the nature of the facts and their effect on the mind. When fresh illustrations of a thought produce familiarity with the idea and thus render it more easily reproduced, it is well. This is true of making a diagnosis or watching an operation but it is not true of striving to memorize more facts than the mind can retain; and medical knowledge has far passed that point today. Therefore the selection of basic topics ought to replace the attempt at omniscience.

There is a disadvantage in the length of medical education, and that is the late age at which the physician is able to begin active practice. He gets through medical school and hospital not earlier than 26—far older than a man ought to be when he begins his work in life, and in most cases too near the end of the age of greatest intellectual fertility.

At the other end of his career, if he has an appointment in a hospital he loses it, as a rule, at 62; and very commonly his private practice therewith. Perhaps the age of retirement is too early or too late—too early if it means withdrawing from the community the benefit of his experience, too late if it means turning over to his juniors the bulk of the work at the hospital while retaining some supervision and a sufficient teaching clinic.

As things stand, the man with a permanent hospital appointment—out of a useful life which could last, let us say, on the average until 70—has a maximum of some thirty-six years for conducting a practice to which he has devoted, including the two premedical years, a minimum of eight years to professional training. That seems disproportionate; what is more, the length of training has been increasing and the age of hospital retirement becoming lower.

In the last half century the age of entering Harvard, and no doubt other colleges, has been reduced almost exactly one year: from 19 and

three months to 18 and three months. I should like to see it fall six months more, for I think reasonably intelligent young men are capable of excellent intellectual development at that period of life. I should much regret to have the students of our best medical schools lose the benefit of contact with other young men in a college of liberal arts, the more so because I lament the withdrawal, as compared with former times, of the physicians from civic affairs, to which they could contribute much.

One who has had a chance to see the medical school only from the faculty table may get impressions of value because he is detached from the interest of teachers in their fields. One sees that interest in the planning of the present Harvard Medical School with four separate establishments for the four chief laboratory subjects, each capable of containing an entire class, with its big lecture room unused three fourths of the time. The impression is that those who planned the school intended to exclude from anatomy and from physiology, for example, any infiltration of the other as something alien to its nature. The old conception was the attainment of medical knowledge by study of many separate fields; that of the present is correlating those fields into one great subject of medicine as a coherent whole.

Formerly the laboratory and clinical professors sat on opposite sides of the faculty table, and if an additional appointment was made to one group it was expected by the other also, that the balance might be maintained. Such an attitude is inconceivable today. The clinic makes constant use of a laboratory, and the laboratory teacher appreciates more fully that his aim is to fit men for practice.

The interest of the medical teacher in his own field as something distinct from medicine as a whole has been greatly reduced, partly at the Harvard Medical School by the general examination for graduation, which has caused both student and teacher to correlate laboratory and clinical knowledge in a striking way. It is strange that this highly effective device has been little copied in other medical schools, for people still regard examinations mainly as a test of work done, whereas their most important function is setting a standard of accomplishments.

For a nonprofessional observer to tell experts how to improve their methods would be presumptuous, but he may properly observe that the results are in some respects defective from the standpoint of the community and of the profession.

Vast improvements in medical education have been made in the last half century but there seems to have been a tendency to add the new to the old without eliminating some things no longer needed.

THE GENERAL PRACTITIONER AND MODERN MEDICINE

Abstract of an article by Dr. J. P. Simonds, professor of pathology, Northwestern University Medical School, published in the June 1940 issue of the Marquette Medical Review.

Medicine has always been interested in everything that can influence the well-being of mankind. The modern physician, especially the general practitioner, must be something of a botanist to understand an ailment so common as hay fever; something of a zoologist to appreciate the relation of parasites and disease; a physicist to comprehend the electrocardiograph, the action and defects of x-rays and radium; a chemist to grasp the underlying conditions of diabetes and exophthalmic goiter; an anatomist to know where to look for an inflamed appendix; a physiologist to distinguish between the normal activities of the body and its disordered functioning in disease; a cytologist to understand cancer; a pharmacologist to know how drugs may influence disease. He must be something of a herpetologist if he practices where poisonous snakes are abundant; a bacteriologist if he is to understand infectious diseases; a diplomat who can say just enough to be within the truth, but neither too little nor too much to do harm in an inquisitive patient; a psychologist in order to understand the whims of his patients; a moralist with high ideals of personal conduct; a humanitarian who loves his fellow men, and a good Samaritan to the suffering.

CRITERIA FOR SUCCESS IN GENERAL PRACTICE

Only the most brilliant men in medicine should go into general practice. Even low grade mediocrity often succeeds in a specialty; only the most intelligent, alert and active minds can attain real success in general practice. This is not a field into which graduates in medicine should drift just because they have not the intelligence, the ambition or the energy to enter a specialty; it should be undertaken as a matter of definite choice with a full knowledge of its requirements, its possibilities, its demands.

But the specialist has an important place in the practice of medicine. When the general practitioner has, after a complete study of a patient, arrived at a correct diagnosis, he may not have the opportunity or the time to develop the skill necessary to do a delicate and extensive operation. Then he calls in a surgeon. But he should be able to tell the surgeon all about the patient and his condition and he should know as well as or better than the surgeon what should be done for the patient. The general practitioner cannot in such instances complete his work for his patient unless he does call in a specialist. He is like the architect, who, with his wide knowledge of stone and steel, plumbing

and electric wiring, heating and ventilation, cannot bring into being the magnificent building unless he has the help of the man with the steam shovel to make the incision in the earth for the foundation and the structural steel worker to put in place the beams which bind the whole together.

THE GENERAL PRACTITIONER

Modern medicine is appalling in magnitude. Discoveries of new methods, new remedies, new active principles are made rapidly. The specialist has only an advancing margin of medical progress to keep up with, but the general practitioner must cover the entire field. By what criteria can the general practitioner determine what is of value among the unrelated tidbits of new medical knowledge published in countless contributions in medical journals? The "reviews" that form an important part of the medical literature today are not always helpful. Often they are mere catalogues of results of observations and experiments, without any any attempt to assign them their position in the framework of modern medicine. For acceptance of what he reads the general practitioner will have to depend on his common sense, his intuition, a sense of fitness and his knowledge of correlative facts.

Medical knowledge exists in strata. Some has been deposited for a long time and is fully consolidated and therefore a sure foundation for practice. Other strata are in process of being laid down and are often disturbed by the ebb and flow of the tides of new discoveries. One must learn to recognize medical truth in both its filmy costume of the abstract as well as in the homely dress of the practical. Truth is discovered in a variety of ways.

Modern medicine is highly mechanized. Both patient and doctor lose much as a result of this change. Many teachers today, especially in the clinical branches, are poor examples to students of what a general practitioner should be. They have lost the self dependence and self confidence that characterized doctors of former generations. Today the physician who is the model of medical students sends his patient to the hospital, where some one in the laboratory makes an x-ray film and reports his observations, the cardiologist interprets the electrocardiogram, the pathologist diagnoses the sections of a tumor removed, a technician determines the nonprotein nitrogen of the blood and does a blood count and a urinalysis. After these experts have given the doctor the benefit of their experience in making a diagnosis, why should he do any thinking in the case? Why should he listen with utmost care to the chest and percuss the borders of the heart? The roentgenologist will tell him whether the heart is enlarged and if so whether it is a mitral or an aortic type of enlargement or whether it is due to a cardiac aneurysm following coronary thrombosis. The roentgenologist will tell him whether there is tuberculosis, a tumor or pneumonia in the lung or fluid in the chest cavity. The intern or the resident takes the blood pressure; the nurse takes the temperature. The older doctors, using their own thoroughly trained five senses, determined most or all of these physical signs of disease themselves about as accurately as it is done today with the modern mechanical devices. And, unfortunately for both patient and doctor, the patient has to pay for all of this laboratory and x-ray work and, no matter how reasonable the doctor's fee, the patient and his family frequently feel that they have been unjustly treated.

The general practitioner, if alert, will learn how to do without many of the mechanical adjuncts of medicine. He will gain in self confidence and in self respect, he will win the respect and confidence of his patients as well as their gratitude because of his fair treatment of them financially, and he can be just as good a doctor as his more highly mechanized teachers.

OPPORTUNITY TO SAVE MEDICINE FROM SOCIALIZATION

We hear much of socialized medicine. The practice of medicine, because of its intimately personal nature, cannot be successfully regimented. Of all our citizens, the general practitioner can do more to save our threatened system of free enterprise than any other single group. When general practitioners tell their patients what the loss of our system of free enterprise will mean to them and to every one in this country, what meddling with the practice of medicine by bureaucrats will mean to the health of their children and their community, how socialization or state control of medical practice might well be a prelude to the complete destruction of free enterprise, they know that what he says is true. The general practitioner occupies not merely a strategic position in this changing world but he can, more than most groups, control the direction and extent of the change that must come with changing conditions. His quiet comments and advice, his reputation for justice and fair dealing, his common sense will do more to prevent the disasters that would follow the regimentation of medicine under the state or under any alien social order than any other one social force.

General practice is the very foundation of the science and art of medicine in this country. The work of the general practitioner is the criterion by which may be judged the quality of the medical service of any community. He is the strongest line of defense against the

invasion of medical practice by those who are untrained and unqualified either to render or to control such services. He will be a strong force in maintaining our system of free enterprise. In paraphrasing the words of Goldsmith:

Ill fares the land, to disease and death a prey,
Where bureaucrats accumulate and doctors decay.

FUNCTIONS OF THE PRECLINICAL SCIENCES

Abstract of an article by Dr. Magnus Ingstrup Gregersen, professor of physiology, Columbia University College of Physicians and Surgeons, and published in Science, March 29, 1940.

The general purpose of a medical school is to train physicians. This training is constantly undergoing changes resulting from advances in science. The student must realize at the start, therefore, that he must obtain a foundation which will not crumble under these advances. He must develop a capacity to alter his concepts according to new facts and establish the habit of assimilating facts in a way that will increase his confidence even as he finds some of his earlier training misconceived. Much of what he will learn rests on insecure experimental evidence. Other phases of his work will be well founded. He must learn to distinguish between the two. This he can do only by drawing his own conclusions from what he regards as well established facts. Such a scientific attitude is the student's most valuable weapon.

A large part of the medical course is devoted to studies in which the student has no contact with patients. These studies are designed to give an understanding of the structure and function of the body. For this purpose medical schools support large faculties and expensive laboratories.

The emphasis on research in preclinical departments is criticized by those who do not fully understand the relation of these sciences to experimental medicine and to the intent of faculties of medicine in training students. The spirit of research has a vitalizing effect on the teaching staff. By stressing this experimental attitude in teaching students the preclinical sciences fulfil their most important function in medical education.

The part of the laboratory is to train the student to make his own observations, in order that these may form the groundwork on which he builds his knowledge. In many instances the technics he employs are also to be his tools in clinical studies, and it is important that he examine them critically. Above all, the purpose is to establish confidence in his power to observe and to reason correctly from his observations. This can be accomplished only by practicing the experimental method.

A phase of teaching about which there is a difference of opinion is the writing of theses based on the reading of original articles. Scientific literature is vast. Practice in finding one's way in it, learning to get the gist of articles without great waste of time, is a necessary part of medical training. Students who depend solely on textbooks miss the flavor of scientific inquiry. The medical curriculum makes heavy demands on students. How to keep them from becoming confused and swamped is a problem that falls mainly to the lot of the preclinical departments, which they meet in their first year.

I cannot overemphasize the necessity of correlating facts from the very start of your course. Don't expect to see or be shown at once the relation of each detail to the practice of medicine. You cannot start at both ends at once. Begin with the small circle of facts under immediate observation and let the extent of your attempts to correlate grow with your acquisition of knowledge. Gradually will come general principles which will serve to simplify the learning process.

Stimulation of the student's will to learn is the chief purpose in pointing out the practical application of certain facts to medical problems. One must not devote too much time to this approach in the preclinical courses, for it may focus the student's attention on specific facts that happen to be of immediate practical value rather than on knowledge of the science as a whole. Failure to observe the difference between fact and its interpretation has caused many needless controversies. You will find that there are contradictions in the opinions and interpretations of instructors in different departments. These need not be a source of confusion, provided we agree on the facts. Some professors impress their opinions on students with such authority that these opinions are regarded as unalterable facts. We must guard against this tendency, for nothing is more destructive to the freedom of thought and creative thinking, the very qualities we aim to encourage. The student must never feel that he will be penalized for expressing an honest well founded contrary opinion in our midst.

DO YOU KNOW WHAT PHYSICIAN—

1. Wrote "The Chambered Nautilus"?

2. Was a candidate for the nomination for President of the United States in 1920?

3. Designed the United States Capitol in Washington, D. C.?

The answers are on page 2238

Medical College News

Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items for consideration for publication in the Student Section.

Columbia Students Assisted

In the annual report for the year ending June 30, 1940, the dean of Columbia University College of Physicians and Surgeons, New York, states that during the year 115 students received scholarships and grants totaling more than $40,000. The average award was $354. Many of the students obtain employment during vacations, and even a larger number work throughout the school year in order to continue their studies. More than 50 per cent of the entire student body has been assisted by scholarships, loans and employment. It is to be hoped, the dean says, that more financial aid can be obtained for the students who have a class, hospital and clinic schedule which makes remunerative employment difficult, to say the least, and who face long internships and hospital training which make substantial borrowing undesirable. Scholarship aid is by all criteria the most satisfactory manner of helping many deserving young men and women ambitious to render public service through some phase of medical practice, science, teaching or health work.

Johns Hopkins Medical History Club Celebrates

The famous librarian Dr. John S. Billings in 1889 brought from the Surgeon General's Library in Washington, D. C., to a meeting in Baltimore several rare medical publications and manuscripts, an incident which stimulated interest in medical history and led to the establishment by Drs. William Osler and William Welch of the Johns Hopkins Medical History Club, which celebrated its fiftieth anniversary November 18. Osler was unfailing in his attendance at the meetings of this club, and it was on these occasions that such well known essays as "The Alabama Student," "Thomas Dover," "John Keats, the Apothecary Poet" were presented before the students and others in attendance.

Jobs for College Students

More than 150,000 young people are being enabled to continue their education in the nation's colleges and universities during the present academic year through jobs provided under the college and graduate work program of the National Youth Administration of the Federal Security agency, it has been announced. Colleges and universities have been assigned employment and fund quotas on the basis of 9.47 per cent of the total number of resident undergraduate and graduate day students from 16 to 24 years of age, enrolled as of Nov. 1, 1939, and carrying at least three fourths of a normal schedule. For the academic year 1940-1941, the national student quota is 101,846. Figures compiled as of April 1940 show that the National Youth Administration paid an average monthly wage of $13.46 to college and graduate students participating in the program. The average wage of the undergraduate was $13.25 a month, while that of the graduate student was $21.78. Undergraduate college students are permitted to earn an amount, established by local authorities, between a minimum of $10 a month and a maximum of $20, while graduate students may earn from a minimum of $10 to a maximum of $30.

The total allotment of college and graduate work funds for the academic year 1940-1941 amounts to $13,713,225. The allotments to the states are made on a monthly basis, usually over a nine month period; however, in some instances the institutions operate on an eight month basis and are allotted funds accordingly.

Young people between the ages of 16 and 24, inclusive, who need assistance in order to continue their education are eligible for employment on the NYA college and graduate work program, which operates in nonprofit-making, tax-exempt, bona fide educational institutions. Officials of each institution have the responsibility for selecting the students and for supervising their work, which includes research and laboratory work, building and repair of equipment, construction and repair of buildings and other school facilities, clerical and stenographic work and library assistance. A total of 1,712 institutions participate in the college and graduate work program.

Hospital Residents Present Programs

Residents of St. Louis hospitals were invited to present the program before the St. Louis Medical Society, November 12. Participating from Barnes Hospital were Drs. William R. Arrowsmith and Samuel P. Harbison, speaking on "Reasons for the Failure of Iron Therapy in Certain Cases" and "Crystalline Sulfanilamide and Wound Healing" respectively; from City Hospital, Dr. Leo V. Mulligan, "Major Amputations in Gangrene of the Lower Extremities," and from Firmin Desloge Hospital, Drs. Henry E. Oppenheimer and Joshua E. Jensen, "Observations on the Effect of Vitamin K" and "Thrombocytopenic Purpura—Relieved by Splenectomy—Report of a Case" respectively.

West Virginia Seminars

At the regular seminar at West Virginia University School of Medicine, Morgantown, November 12, the student body was addressed by Dr. William L. Mullins, assistant professor of medicine, University of Pittsburgh School of Medicine, on heart disease; in the seminar October 25, by Dr. Edward G. McGavran, county health officer, on functions of county health departments as they relate to the practice of medicine, and at that on October 11, by Dr. George R. Maxwell, Morgantown, on the heart in the practice of medicine.

Harvard Class Plans Gift to School

The class of 1925 of Harvard Medical School, Boston, at its reunion in New York in June enthusiastically approved the proposal that the class raise $10,000 to be given to the medical school at the class reunion to be held in 1950, the money to be invested by the university and the income to be used for the medical school.

Applicants for Admission to Columbia

The dean of Columbia University College of Physicians and Surgeons, New York, Dr. Willard C. Rappleye, in his annual report for the year ending June 30, 1940, states that 413 students were enrolled in the regular course for the degree of doctor of medicine during the year, of whom 103 were seniors and 107 freshmen. There were 1,048 applicants for admission to the first year class. The students had prepared in 163 different colleges and universities. The class admitted during the year had prepared in forty-seven colleges. The graduating class obtained internships

in fifty-three different hospitals in all sections of the country. One hundred and ten students who were registered under the graduate faculties of the university took their work at the medical school during the year. Instruction in the medical sciences for the school of dental and oral surgery was provided for the students of that school. There were 194 residents in the hospitals affiliated with the graduate medical program, of whom fifty-two were registered for the degree of doctor of medical science. In the postgraduate courses offered at thirteen hospitals, 1,061 physicians were registered from forty-three states and twenty-three foreign countries.

Dr. Gates Addressed California Seniors

Senior students at the University of California Medical School, San Francisco, the faculty and guests were addressed in November by R. Ruggles Gates, Ph.D., LL.D., professor of botany, King's College, University of London, London, England, on "The Biology of Human Blood Groups." Dr. Gates in 1915 lectured at the Genetics Congress in San Francisco and in that year published his book, "The Mutation Factor in Evolution"; in 1916 and 1917 he was acting professor of zoology at the University of California. In 1929 he published a reference book on heredity in man and became deeply interested in human blood groups, which during his extensive travels he investigated in various native peoples in South America, India and Canada.

Tufts Scientific Forum

The Scientific Forum at Tufts College Medical School, Boston, is an organization that gives students an opportunity to present papers. The following students presented papers before this group during recent weeks: Alfred G. Chandler '42 on "Diagnosis of Brain Tumors"; Robert W. Riemer '42, "Nervous Indigestion"; Jerome C. Saltz '42, "Specific Treatment of Chronic Arthritis," and Dudley B. Tyson '42, "Psychoneuroses as Seen in General Practice." The president of the Scientific Forum this year is Robert W. Riemer.

Field Day at Wisconsin

To promote fellowship and better understanding between the teachers and students at the University of Wisconsin Medical School, Madison, is the object of the annual field day which is held in the spring. The day begins with a review of research being carried on by students. There are special exhibits, a luncheon, then an address by some well known guest. The respective classes give vent to their rivalries in base ball games in the afternoon and finish the day at a banquet which both faculty and students attend.

Music Room for Harvard Students

A music room has been fitted out in the students' dormitory, Vanderbilt Hall, at Harvard Medical School, Boston, for the comfort and entertainment of students, and the library has been redecorated with new lights and new chairs. The dining room rates have been changed, so that more students may be able to take their meals there.

California Lecture

The senior students and faculty of the University of California Medical School, San Francisco, were recently addressed by Wendell L. Stanley, Ph.D., of the Rockefeller Institute for Medical Research, N. Y., on the subject of viruses. Dr. Stanley during this semester is Hitchcock Lecturer at the University of California.

Duke Premedical Student Wins Scholarship

Joseph W. Taylor Jr., Tampa, Fla., a premedical student at Duke University School of Medicine, Durham, N. C., has been awarded a tuition scholarship at Duke as one of five members of his class having the highest averages. According to the Tampa *Tribune*, Mr. Taylor is also a member of Phi Beta Kappa and of other honorary clubs and a member of the Duke University golf team.

Tennessee's Comprehensive Examinations

When a student at the University of Tennessee College of Medicine, Memphis, completes the first six quarters of the medical course, the privilege of registration in the seventh quarter is withheld for one quarter until the student is given a comprehensive examination on the preclinical courses by a committee appointed from the clinical staff. The object is to determine the student's fitness to undertake the clinical courses. The examinations, which require three nights to complete, are individual and oral. The winter comprehensive examinations at the University of Tennessee College of Medicine will be held Jan. 2-4, 1941.

"DO YOU KNOW WHAT PHYSICIAN"

Following are answers to the questions appearing on page 2236:

1. Oliver Wendell Holmes, who for thirty-five years was professor of anatomy and physiology at Harvard. In 1843, while still a medical practitioner in Boston, Holmes reported his discovery of the contagiousness of puerperal infection. These observations were confirmed several years later by a young Hungarian physician, Ignaz P. Semmelweis.

2. General Leonard Wood, who graduated from Harvard Medical School in 1884 and for many years served in the medical corps of the U. S. Army. Later he was transferred to the line and became chief of staff of the army and governor general of the Philippine Islands. General Wood died in Boston in 1927.

3. Dr. William Thornton. In October 1792, Dr. Thornton requested from the commissioners an opportunity to present a plan; his request was granted and his plan accepted by the commissioners April 5, 1793. Some fourteen plans for a capitol building had been submitted by others previously, but none was wholly satisfactory. In the development of Dr. Thornton's plans in the erection of the first unit of the Capitol Building, three architects were employed—Stephen H. Hallett, George Hadfield and James Hoban, the architect of the White House. The erection of the south section of the Capitol, which is now occupied by Statuary Hall, was under the charge of B. H. Latrobe. The dome of the original central building, constructed of wood covered with copper, was replaced in 1856 by the present structure of cast iron, completed in 1865. The dome receives light through 108 windows. Dr. Thornton was born in 1761 on the Island of Tortola, West Indies, and received his M.D. degree in Edinburgh in 1784. He continued medical study in Paris and then came to Washington, D. C. He served as the commissioner of the District of Columbia for eight years. President Jefferson appointed him clerk of patents, and later he became the first commissioner of patents. Dr. Thornton became a member of the Medical Society of the District of Columbia in 1819, the year in which the society received its first charter from Congress, and was vice president of the society 1820-1823. He died, March 28, 1828 and was buried in the Congressional Cemetery.